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ORIGINAL ARTICLES

THE HISTOGENESIS OF CANCER OF THE STOMACH.[1]

By William Carpenter MacCarty, M.D.,

MAYO CLINIC, ROCHESTER, MINNESOTA.

It is generally thought that gastric carcinoma arises from post-natal epithelial rests which are supposed to be present either in

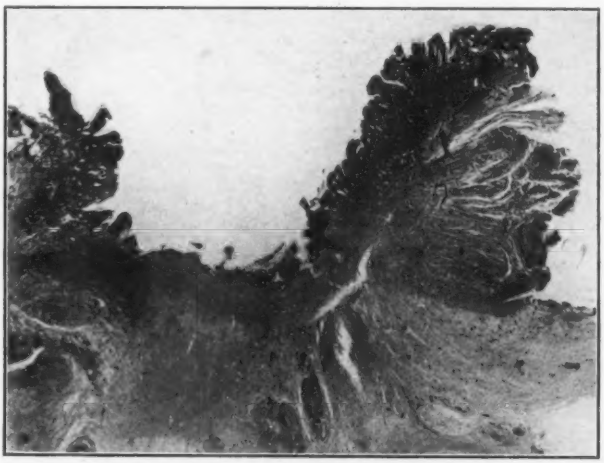


Fig. 1.—Low-power photograph through a section of a simple chronic gastric ulcer.

the scar-tissue bases or the submucosa of gastric ulcers. Since this idea is theoretical, I take the liberty of presenting briefly

[1] Read before the Academy of Medicine, Kansas City, November 20, 1914.

some facts relative to the histogenesis of gastric carcinoma and its relation to gastric ulcer.

Simple chronic gastric ulcers have never, in my experience,

FIG. 2

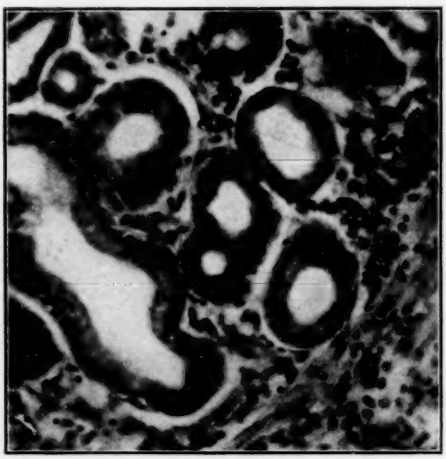


FIG. 3

FIGS. 2 and 3.—Photographs through the border of a simple chronic gastric ulcer. The glands are regular and show little or no distortion. The cells are regularly arranged around the lumen. The nuclei occupy a basal position in the cells.

presented any visible epithelial rests which one could scientificially state were prenatal. Neither have I seen postnatal epithelial rests in the mucosa, submucosa, or ulcer base that were not either com-

posed of atrophic epithelium or real carcinoma, the latter condition being present in the base or submucosa only when there was extensive involvement of the mucosa.

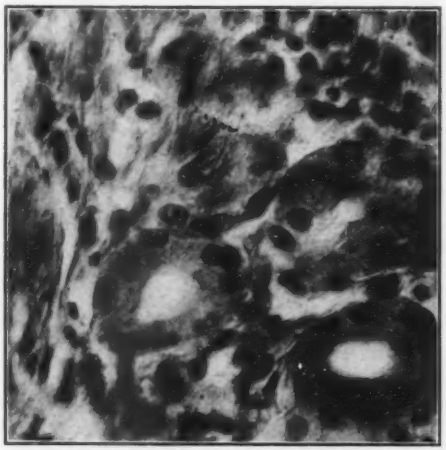


FIG. 4.—Photographs through the same border from which Figs. 2 and 3 were taken. The cells do not present the regularity of arrangement seen in Figs. 2 and 3. The nuclei are not regularly placed at the bases of the cells. They vary in size and shape.

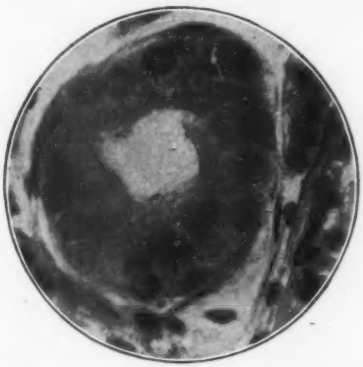


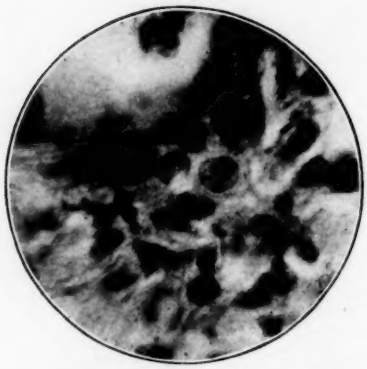
FIG. 5.—Several glands showing the same cytological changes which are seen in Fig. 4. This picture is frequently found in simple chronic gastric ulcers and presents the same cellular appearance which is seen in secondary epithelial hyperplasia in the breast, prostate, skin, and hair follicle.

In the simple chronic ulcer (Fig. 1) one frequently finds the glands composed of columnar or cuboidal cells, regularly arranged with oval or round nuclei, which are almost always of the same

size and are placed near the bases of the cells (Figs. 2 and 3). The cells are sharply demarcated from the stroma, which consists of fibroblasts, differentiated fibroblasts, and some lymphocytes, all of

FIG. 6

FIG. 7



FIGS. 6 and 7.—Intraglandular epithelial hyperplasia similar to that in Figs. 4 and 5 plus extraglandular epithelial cells which are morphologically similar to the intraglandular cells.

which form a histological picture distinguishable from the normal gastric mucosa with great difficulty. From this picture to carcinoma there are transitional apparently intermediary pictures the extremes of which are easily distinguishable.

The epithelial cells of the glands in some ulcers lose their cuboidal or columnar shape and regularity in size and arrangement (Figs. 4, 5, 6). They become oval or round and the nucleoli become larger and more distinct. The exact origin of these cells is at present unknown, since in the gastric gland there are not two distinct rows of cells normally present, as in the breast, prostate, skin, and the accessory epithelial organs of the skin. To my knowledge, a germi-

FIG. 8

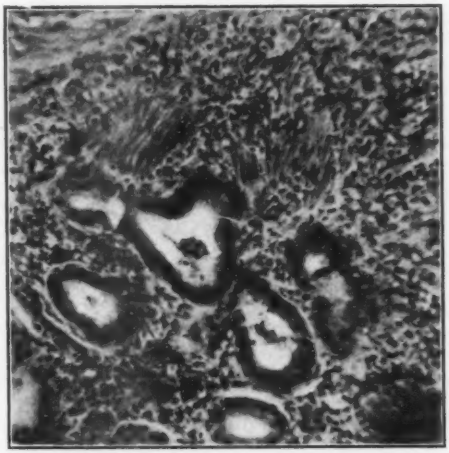


FIG. 9

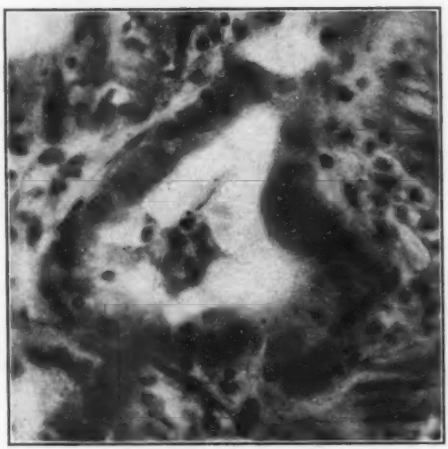


FIG. 10

FIGS. 8, 9, and 10.—Three magnifications of the same gastric gland showing an intraglandular cytoplasia in the mucosa of a chronic gastric ulcer. The cells if compared with those in Figs. 11 and 12 will be found to be indistinguishable.

native layer of cells or a germinative focus of cells has not as yet been satisfactorily demonstrated.

The cells (Figs. 5, 6, 7, 8, 9, 10) which are frequently found, however, present a morphological picture which is indistinguishable from that seen in secondary epithelial hyperplasia in other organs having a germinative layer which is the origin of cancer cells.* Various degrees of intraglandular morphological changes (Figs. 5, 6, 7, 8, 9, 10) are found in the borders until the cells become indistinguishable from cancer cells (Figs. 7, 11, 12, 13). When such a condition is found, careful search frequently demonstrates a lack of demarcation between the gland and the stroma, and epithelial cells may be seen in the stroma, the later condition being accepted by general pathologists to be the histological criterion of cancer. When cancer is definitely present in the mucosa or other coats of the stomach the intraglandular cells always present the condition which has been described as secondary hyperplasia in other organs.

From a cytological standpoint I see no objection to denoting the condition as secondary hyperplasia in the stomach. It is apparent that the histogenesis of cancer in the stomach bears an analogy to that in the breast, prostate, and skin, with the one exception that the germinative stratum or focus has not been demonstrated, a condition which differs from primary epithelial hyperplasia in the organs just mentioned.

* See appended references.

In the production of these apparent stages of epithelial hyperplasia whatever the irritant or irritants are, be they extrinsic or intrinsic, there is an apparent attempt on the part of nature to

FIG. 11

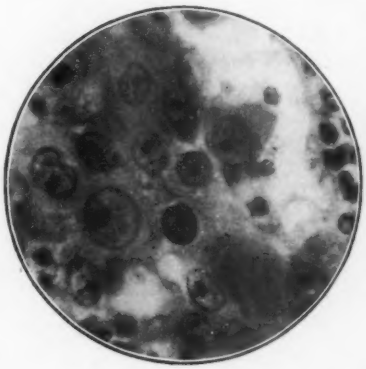


FIG. 12

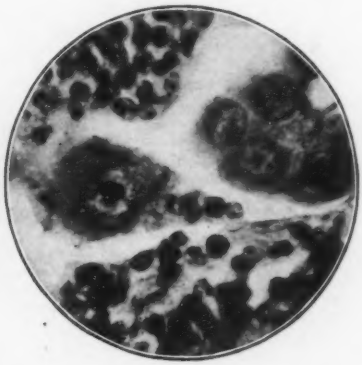
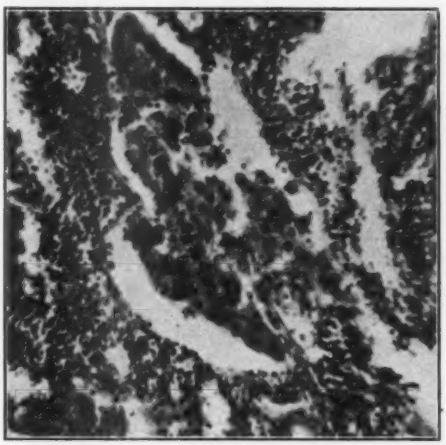


FIG. 13



FIGS. 11, 12, and 13.—Cells from a carcinomatous involvement in a subpyloric lymph gland in a case of gastric carcinoma. The cells are morphologically indistinguishable from the cells of an intraglandular cytoplasia which is frequently seen in simple chronic gastric ulcers.

reproduce the epithelial lining of the glands. In this attempt there is failure to completely differentiate the cells with the coincidental picture of secondary hyperplasia the cells of which differ from cancer cells only in position.

From these facts one may clearly see that the gastric cancer cell arises from intraglandular hyperplastic cells of the mucosa, and represents a malignant end-stage of a process of hyperplasia of normal cells.

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PERFORATED GASTRIC AND DUODENAL ULCER.

By George G. Ross, M.D.,

PHILADELPHIA.

In the whole field of surgery I know of no condition in which more depends upon prompt diagnosis and immediate intervention than in cases of perforated gastric and duodenal ulcers. The treatment of such ulcers in the absence of perforation is still open to discussion—our course when we have to deal with a perforation is plain and we need concern ourselves only with the features of the diagnosis, the operative technique, and the postoperative treatment. I believe also that the symptoms of a perforation of the stomach or duodenum are practically always of such a nature that a diagnosis should be possible without delay, although in a few instances the course of events has been so different from what one might be led to expect that an exact differentiation has been difficult. But in every instance I am certain there is sufficient warrant for the belief that some pathological condition within the abdomen exists which demands prompt operation, unless the case has survived the first few days and the symptoms become masked.

It has been my good fortune lately to see a considerable number of most interesting cases of perforated ulcer, and I cannot do better than to demonstrate the points I wish to make by a direct reference to the case histories. The first case was seen by me in consultation, was referred to the wards of the German Hospital, and operated on by my chief, Dr. John B. Deaver, during his clinic the same afternoon. This was a case of perforated duodenal ulcer. The history is as follows:

H. A. S. was operated on November 15, 1913. His previous history shows that seven or eight years before the present illness he had an attack of indigestion which lasted for several weeks. Three months before his perforation he began to have an uncomfortable feeling of fulness in his stomach, coming on immediately after eating. This condition was relieved by restricted diet. He was never able to belch and never vomited; was constipated and flatulent. Used alcohol moderately. On November 14, 1913, he ate a heavy lunch, and was very uncomfortable during the afternoon. At about 6.30 P.M. on the same day, while sitting at a desk writing, he had a severe attack of epigastric pain, coming on suddenly and radiating up over the chest. The pain was constant, not spasmodic, and was made worse by inspiration. There was no nausea, but the patient tried to induce vomiting in the hope that it might relieve the pain. The pain kept up all night, and was referred also to the back of the neck and right shoulder. The next morning he drank a glass of warm milk and retained it, and his pain was not aggravated by it. I saw the patient the morning after the onset of his acute illness. The abdomen was distended and there was a general board-like rigidity. There was tenderness, its point of greatest intensity being midway between the umbilicus and xiphoid. The liver dulness was diminished. Peristalsis was present. The leukocyte count was 23,500, with 89 per cent. polynuclears. I advised immediate operation upon the diagnosis of perforated ulcer.

At operation an appendectomy was first performed, gas and cloudy serum escaping when the peritoneum was opened, and purulent material appeared when the adhesions about the appendix were broken up. An upper right rectus incision was then made and a perforation of the posterior surface of the duodenum was found. The duodenal opening was closed with linen-thread suture and the gastrohepatic and gastrocolic omentum stitched over it. The duodenum was plicated and a posterior gastro-enterostomy done. The upper abdomen and pelvis were cleaned with gauze pads and a glass tube put in the pelvis for drainage. The patient made an uninterrupted recovery.

This case may be taken as a typical one. Not having seen him earlier, I did not have the clinical picture presented shortly after perforation, but the history approaches a classical one.

First we have a clear history of antecedent trouble, with a long intermission between the two attacks. Next there is the history of a prodromal period of a few hours before the actual perforation. It is true that often a perforation of a gastric or duodenal ulcer comes without any warning, but premonitory signs are not infrequent. In practically every instance we can find, by careful questioning, there is a definite if not typical history of digestive disturbances at some time in the patient's career.

The physical signs on the following day were exactly what one would expect. The patient had evidently suffered some grave accident. The abdomen was rigid. This board-like rigidity is a marked feature of the perforation of upper abdominal ulcers. At first we usually note only a marked rigidity of the upper recti—a sign almost pathognomonic when it is typical.

In the case just described an error in diagnosis would have been difficult. Moreover, in the presence of such a history of digestive disturbances entirely different from that encountered in chronic gastric ulcer we were correct in diagnosing a perforated duodenal ulcer.

Another of my recent cases is even more typical, and was seen earlier in the course of the illness.

E. McC. was admitted to the Germantown Hospital, February 28, 1914, at about 2 A.M., suffering with intense upper abdominal pain. The previous afternoon, while at work lifting a heavy bar, he was taken with a sudden, sharp pain in the epigastrium. After treatment by a druggist with salts and gastric lavage by his doctor —in the course of which much fluid was put into the stomach and but little gotten out—he came to the Germantown Hospital. A diagnosis of perforated gastric ulcer was made on the history, marked abdominal rigidity and distention, rapid pulse, and leukocytosis of 24,000. In this case we could not obtain a history of previous gastric disturbances.

At operation, upon opening the peritoneum, large quantities of gas and stomach contents escaped. It was some time before the perforation could be located, upon the anterior wall about one and one-half inches from the pylorus. It was closed and a gastroenterostomy performed, because the induration to the pylorus and the closure of the ulcer considerably lessened the lumen of the stomach at this point. A pelvic glass drain was inserted and the upper wound closed with cigarette drainage.

Here again we have a typical case of perforated ulcer, but a gastric one. There was, however, absolutely no history of antecedent illness. Mr. Paterson states that it is always easy to distinguish between a perforated duodenal and gastric ulcer, but I have not found it so. In later cases the diagnosis presents an entirely different problem. We do not have the early physical signs to correlate with the history.

Thus a case coming under my care in the Germantown Hospital on January 26, 1914, well illustrates these points:

M. S., female, aged sixty-eight years, gave a history of stomach trouble since childhood, having spells of indigestion coming on three or four hours after eating and causing vomiting. These had been more marked within the past three years, coming on every six or seven weeks. One week before admission such an attack occurred, on Monday, January 19. The following Thursday

she had to go to bed, and on Sunday, January 25, she suffered intense abdominal pain, with vomiting. This continued with little cessation up to the time of admission. The bowels did not move for seven days prior to admission. Physical examination showed the patient to be poorly nourished. The abdomen was tender, but very little distended. There was visible peristalsis, and knuckles of gut could be seen through the relaxed abdominal wall. Vomiting ceased upon absolute starvation. Intestinal obstruction was suggested as a diagnosis, but my diagnosis was a malignant growth of the sigmoid with partial obstruction. After several days' delay I operated and made a rectus incision. There was no evidence of disease in the lower abdomen. A knuckle of ileum was found adherent to the stomach at the pylorus, kinked, and giving rise to mechanical obstruction. This being freed a perforation of the anterior wall large enough to receive a lead pencil was exposed, with no peritonitis about it. It was closed by purse-string suture, etc., and reinforced by an omental graft. The wound was closed without drainage, and the patient made a good recovery.

Here we had a most interesting case from the standpoint of diagnosis. The history of antecedent illness was direct and to the point—a history of ulcer. The onset was subacute, and the progress of the case delayed because a spreading peritonitis was avoided. The second and later pain was that of the obstruction, which also caused the vomiting. Rigidity and marked tenderness were absent because there was no peritonitis.

This really was a case of perforated gastric ulcer in which a diagnosis would have been difficult at any time because of the prompt blocking of the ulcer. At the time of admission an absolutely positive diagnosis could hardly have been made at all, as all symptoms were masked by those of the complicating obstruction.

In instances in which there is but a few days' delay we still have our guiding-points in diagnosis. Another case operated on at the Germantown Hospital, on February 11, 1914, after two days' illness, still showed unmistakable signs of perforated ulcer, and gave an excellent previous history. At operation, however, it was plain why this should be so, as a subdiaphragmatic abscess was found.

On the other hand we may have to deal with an entirely atypical history.

On March 26, 1914, there was admitted to the Germantown Hospital a man, aged twenty-three years, whose history was as follows: The patient was taken sick March 20, 1914, with a feeling of malaise. On March 21 he became worse, had a chill, and went to bed. Later he felt better and got up. The patient had nosebleed the day before admission. He developed abdominal tenderness the day of admission, with pain in the back of the head and

in the neck muscles, and vomited that evening. He had anorexia, but was thirsty. He had a short, dry cough, with tenacious and bloody (?) expectoration. His abdominal pain made breathing painful. His previous history gave us a clue—a history of hunger pain. The patient when I saw him was feverish. On admission he had epigastric tenderness and slight abdominal rigidity. A mass was felt in the upper left abdominal quadrant extending about 6 c.c. below the costal margin.

Three days after admission, and on the tenth day of his illness, he was transferred to my service. A diagnosis of left-sided subphrenic abscess was made, probably due to perforating ulcer. This was confirmed, but a drainage operation only was possible. The ulcer was not found at operation, but various lymph masses about the anterior and posterior stomach walls were not disturbed. The patient died of general peritonitis. A partial autopsy disclosed a perforation on the posterior wall of the stomach and two of the duodenum. There were two small unperforated ulcers of the stomach near the cardiac end. The perforation into the lesser peritoneal cavity and the localization of the abscess above delayed the end in this case, but the whole is a lesson on the consequences of delay in diagnosis and treatment.

It is not impossible to mistake a perforated duodenal or gastric ulcer for a case of appendicitis. This occurred to me in a case operated on five years ago. I do not think, however, that I would make the same mistake now, particularly in a case seen as early as I saw this one. It must be evident then that in perforated gastric and duodenal ulcer we have a problem difficult but not impossible of a proper solution if it engages our attention at the outset of the condition. It is not my purpose to note the pathology of perforations, their site, or to quote statistical facts. These have all been thoroughly investigated and published in papers easily obtainable, notably one by Elliot in 1912. I wish to consider briefly the diagnosis of gastric and duodenal perforations, their surgical treatment and after-treatment.

The history of previous illness is most important. It is but rarely that we cannot elicit a history definitely pointing to a gastric or duodenal lesion. Great care and persistence are often needed, and often the patient before operation is too ill to give us a good account of his past medical history. It is a noticeable fact that in later years we have been more alert to appreciate points in the previous histories of our patients. The situation parallels that seen in cases of gall-stone disease. Formerly we read and heard much of gall-stones without symptoms. The symptoms were merely unrecognized. So it is with ulcer of the stomach and duodenum.

Of the actual diagnostic points when a perforation of a gastric or duodenal ulcer has occurred we have to consider:

1. The history of acute pain.
2. The presence of marked rigidity of the recti, especially above.
3. The evidences in the patient's general condition that he is quite ill.

The pain accompanying acute perforation is generally described by the patient as excruciating, and is referred to the epigastrium. It sometimes comes without warning, although there are frequently premonitory signs, such as gastric heaviness, distress, or malaise after eating. The pain is of such character and so described and localized that I have been inclined to make the diagnosis thereon in the absence of certain of the symptoms. In the spring of this year a man of middle age, who following several severe attacks of epigastric pain and prostration, came to my attention. Abdominal rigidity was absent, but there was a sense of resistance and tenderness particularly noted upon the right side. There was dulness in the flanks. The patient was not, however, shocked. Leukocytes were 11,000. Operation disclosed the abdomen, greater and lesser peritoneal cavities, filled with bright-red blood and clots. The gastrocolic omentum and transverse mesocolon contained hematomata and the posterior wall of the stomach was infiltrated with blood. The source of the hemorrhage was not disclosed. The man temporarily recovered, but a few months later developed an obstruction in which operation was so long delayed that he did not recover. I had concluded that a perforated gastric ulcer must have eroded the wall of the vessel at the greater curvature to have given us such a hemorrhage, but the pathological report on the stomach does not give absolute proof of this upon gross examination, and the microscopic studies fail to show the signs of a healed ulcer.

The abdominal rigidity is intense and characteristic. At first the abdomen may be scaphoid, but later it becomes distended. The rigidity is always more intense in the epigastrium, but when the peritoneal infection spreads we meet with a general abdominal rigidity. Tenderness accompanies the rigidity. It has been stated that the point of maximum tenderness indicates the site of the perforation, but this I am not able to substantiate. Shock was formerly stated to be an important diagnostic point. I do not find it so. The patient suffering from perforated ulcer is evidently ill, is usually prostrated, and may suffer from true surgical shock. Leukocytosis is present in so many conditions that its diagnostic value is slight. When the perforation is protected or already walled off by adhesions or other viscera the rigidity and great tenderness may not supervene—that is, the symptoms of a peritonitis do not become evident.

In cases which survive and suffer from localized collections, such as a subdiaphragmatic abscess or a diffuse peritonitis anywhere within the abdomen, the local symptoms resultant therefrom will be manifest.

The differential diagnosis of perforated ulcer is not, as a rule, difficult. There are many conditions in which errors have occurred, yet I think not often justifiably so. Because of the severe epigastric pain often associated with appendicitis, this is the incorrect diagnosis most often made. Moreover, if fluid drains from a duodenal ulcer into and through the right kidney pouch tenderness and rigidity may be very noticeable in the right iliac fossa. The history and other symptoms, however, should soon make the correct diagnosis.

Intestinal obstruction with sudden onset may simulate the pain of a perforation—the rigidity and inflammatory signs would, however, be absent.

A ruptured gall-bladder would give identical symptoms. The condition is rare and particularly so without a history of trauma or infectious cholecystitis for some time prior to the perforation.

Acute pancreatitis has its onset with pain like that of a perforation. Here the slow pulse, low temperature range, and evidence of involvement of the lesser peritoneal cavity only, without a peritonitis in the greater cavity give us our clue. Subsequent developments are entirely different also, and the symptom-complex of acute pancreatitis is very definite.

When late complications set in after the perforation of an ulcer the symptoms may simulate those of the same complications, due to other causes, and a differentiation may be possible only in the presence of a definite history.

A diagnosis of perforated ulcer having been made surgical intervention is called for at the earliest possible moment. Delay is fatal.

The anesthetic of choice is ether, possibly with nitrous oxide preceding it. A free incision through the upper right rectus exposes the field. The escape of gas, and especially gastric contents, establishes the diagnosis. Rapidly but gently we search for the site of the perforation, bearing in mind that there may be more than one. If there be fluid in the field of operation it should be sponged away, or if there be tissue masses or food particles normal saline may be used to wash it away. Occasionally, as in one of the cases quoted, the presence of an abscess makes it possible to do only a drainage operation, and the perforation is not located. This, however, is fortunately a rare circumstance. The perforation being found it is closed with a purse-string suture of linen thread, if this is possible, reinforced by Lembert sutures. Or it may be merely sewed over. In either case reinforcement by omental grafts is of distinct advantage. If the surrounding induration is such that a closure by suture is impossible we may have to content ourselves with putting drains to the site of perforation. More extensive operations upon the ulcer-bearing area are contraindicated in the presence of perforation.

The possibility of multiple perforations must not be over-looked. In one of my early cases the perforation of a second ulcer was responsible for a postoperative death.

I believe that gastro-enterostomy should be performed only when by induration or suture the lumen of the pyloric end of the stomach or duodenum is encroached upon. Even then, unless it be absolutely essential, it should not be attempted by an inexperienced operator. Such a one should do as little as possible in every case—close the perforation and drain.

It is true that a gastro-enterostomy tends to cure the ulcer, but it is a formidable operative procedure and not to be lightly regarded in the presence of so acute a condition as perforated ulcer. It tends also to prevent secondary perforations, but even herein is not always effective.

The gastric repair being completed and the toilet of the peritoneum finished the abdominal incision is ready for closure. I drain all my cases by a glass tube into the pelvis placed in a lower abdominal stab incision in the median line. The upper wound may be entirely closed in early cases or drained by a cigarette or gauze rubber tube drain where there has been an abscess. Postoperative treatment is simple. The pelvic drain can usually be removed in forty-eight hours and other drainage in four or five days. The patients are kept upright after coming out of the anesthetic, medicated only when necessary, and supplied with saline freely by continuous or intermittent proctoclysis. Morphin is not harmful in these cases when judiciously used. For persistent postoperative vomiting gastric lavage is employed—the operative procedures on the stomach do not contra-indicate it.

I have recently seen a case which is of such unusual interest that I add it to this paper, as I believe it to be a case of perforated gastric ulcer at the cardiac end of the stomach.

J. F., aged forty years; chief complaint was chronic gastric indigestion for many years. His disposition was irritable and unreasonable, due to his continuous discomfort. As a result of his illness he contracted the alcohol habit and had been treated for it in an institution, but had not taken stimulants for five weeks prior to his acute attack. In addition to stomach dyspepsia he suffered from frequent attacks of abdominal pain and diarrhea.

About 10 P.M. on September 6, 1914, he had an attack of nausea, and vomited. The patient stated that the vomitus looked like blood, but this could not be confirmed. Immediately following the vomiting he developed an extremely severe precordial pain, associated with collapse and marked shock. Morphin in large doses failed to relieve the pain, and measures directed against the shock failed. By 2 A.M. on September 7, 1914, the patient developed evidence of acute pneumothorax. A mass could be made out just below the left costal margin, which was very tender, and over

which the rectus muscle was markedly rigid. By 9 A.M. on September 7, when I first saw the patient with his family doctor, Dr. George Cameron, his condition was as above described, only the shock was more intense and the pain unrelieved. His entire abdomen was tender, but was more intense in the left hypochondriac region. The mass in this locality was readily mapped out in spite of the muscular rigidity. The pneumothorax had increased until the apex beat of the heart was to the right of the sternum. Breathing was labored, and he experienced considerable difficulty on inspiration.

Surgery being out of the question a medical consultant was advised, and Dr. George M. Piersol was asked to see the case. He arrived about 11.15 A.M., and while making an examination the patient expired.

In the absence of tuberculosis and traumatism, except the spell of vomiting, and of cough or bloody expectoration, and with the history of prolonged stomach dyspepsia with pain, a diagnosis of perforated gastric ulcer at or near the cardiac end of the stomach was made. The explanation of the pneumothorax was that the ulcer was adherent to the under side of the diaphragm, and when perforation occurred it included the diaphragm and parietal layer of the pleura.

A postmortem was refused, so that this diagnosis must remain unconfirmed and a matter of speculation. However, the evidence seems sufficient to justify the inclusion of the case in this series.

REPORT OF A CASE OF PAROXYSMAL TACHYCARDIA WITH OBSERVATIONS ON TREATMENT.

By Walter L. Niles, M.D.,

ASSISTANT PROFESSOR OF CLINICAL MEDICINE, CORNELL UNIVERSITY MEDICAL COLLEGE; ASSISTANT ATTENDING PHYSICIAN TO BELLEVUE HOSPITAL, NEW YORK.

The patient, a married man, aged thirty-seven years, has continuously been under my observation since March 18, 1909. Cardiac valvular disea e was first recognized when he was eighteen years of age, and, according to the family legend, he "strained" his heart at about that time, while rowing. Careful questioning fails to elicit a history of any illness which might be interpreted as acute rheumatic fever or any other infection which would be likely to involve the heart. He was a ways extreme y moderate in the use of alcohol and tobacco, and venereal infections were denied.

The first paroxysm of tachycard a came on in 1905, immediately

after "shooting-the-chutes," and during the next six years he experienced many repetitions. The attacks varied in duration from a minute or two to twenty-eight hours, the average being from four to six hours. Their frequency was also variable, sometimes recurring three or four times a day, while at other times there were intervals of freedom lasting several weeks; the longest was nine weeks. These attacks did not appear to be precipitated by any specific cause, although much exertion would quite surely cause one, as would, apparently, any toxemia.

In 1907 he is said to have had a mild attack of "grip," which was followed by jaundice lasting one week, during which time he had a great number of attacks.

I have frequently noted that a mi d coryza, or tracheitis, was likely to be accompanied by paroxysms, and that stasis in the intestinal tract would quite surely precipitate them, often being preceded by a few urticarial spots. I attempted to determine whether any specific protein caused them, but was unable to arrive at such a conclusion. They quite often started at night, and the patient thought they were more apt to occur if he lay on h's left side when sleeping, or they began while working at his office, or while eating. He was always immediately aware of the onset of an attack by a sensation of fulness in his chest and throbbing of his heart. He usually went to bed—if not already there—and sat upright with pillows at his back. He had no dyspnea except in long attacks, but was distinctly uncomfortable if he tried to lie down. After about an hour he would complain of "feeling sick all over," having pain in his head, back, and limbs, and constant nausea with frequent vomiting of considerable mucus. He constantly had a mild degree of icterus, and during long attacks this became deeper.

The attacks always ceased abruptly with a "bump" of his heart, and the pulse would then immediately become slow and regular. Within a few minutes he would feel quite well, and could shortly take food. There were no premonitory signs to indicate either the onset or offset of attacks.

Examination between paroxysms showed a man of spare build and poorly developed muscles, with a faint icterus in the skin and scleræ. The pulse was 72 to 80 per minute, regular, and of normal size and force. The vessels were not palpable. Systolic blood-pressure, 110; diastolic, 75. The heart transmitted a diffuse, heaving impulse to the precordium, the point of maximum impulse being in the sixth left interspace, 11 cm. from the median line. The apex beat was in the sixth space, 13.5 cm. to the left of the median line. There was no undue pulsation of the cervical vessels. The upper border of cardiac dulness began at the second rib, the left border was 14.5 cm. to the left and the right border 5 cm. to the right of the median line. Auscultation revealed a long, low, harsh

systolic murmur, best heard at the maximum point of impulse, which could be traced into the left axilla and below the angle of the left scapula, also over the body of the heart and 3 cm. to the right of the midsternal line in the fifth interspace. A long, rumbling, crescendo diastolic murmur, which ceased abruptly with a sharp, loud shock to the first sound, was also heard over a small area just to the right of the apex beat. The pulmonary second sound was much accentuated. Polygraphic tracings showed normal jugular and radial curves. The lungs and abdominal viscera were negative. There was no ascites or edema, and the urine and blood were normal. Wassermann reaction negative.

During attacks the patient was usually found sitting up in bed, looking sick and anxious, but he was not cyanotic. The whole left side of the thorax would be rapidly heaving, and a wavy impulse was seen in the fourth, fifth, and sixth interspaces. The most striking feature of inspection was, however, exceedingly violent throbbing of the jugular bulbs, which was so great that it was impossible to get tracings directly from them. The systolic blood-pressure was 90 to 95. Except in very long attacks, dilatation of the heart could not be demonstrated. The heart sounds, which were perfectly regular, varied from 140 to 190 per minute, usually being about 170. A short, faint, systolic murmur could be heard over the precordium. The pulse was very small, but there was no deficit.

Since the onset of attacks of tachycardia the patient has led a very quiet life, being largely freed from business cares. A great variety of therapeutic measures for stopping the paroxysms were tried, but none, except that noted later, seemed to be of value if the paroxysms lasted more than an hour. They sometimes ceased, with vomiting or defecation. Pressure on the vagi, changes in position, and prolonged holding the breath were without avail, except the latter, which frequently terminated short attacks and was most relied upon by the patient.

It was difficult to get tracings from the jugular bulbs during paroxysms because of their tremendous throbbing, but those obtained show the ventricular form of the venous pulse (Fig. 1). It is quite certain that the auricle was not fibrillating as the heart was always regular, and Lewis has concluded "That auricular fibrillation is never accompanied by regularity of the ventricle except when it is complicated by auriculoventricular heart-block, and it appears reasonable to assume that when the ventricular form of venous pulse is present and the pulse is regular and of normal or increased rate the auricle is not in a state of fibrillation."

During the fall of 1911 the patient was about as usual, having short attacks every few days until November 13, when he had a paroxysm lasting twelve hours. It was accompanied by no unusual features, and on November 14, although he remained in bed, he

felt perfectly well and reported his heart to have been slow and regular all day. However, at 7 P.M. it became rapid (140 to 180 per minute), and so continued, except for short intervals subsesequently noted, until 8.30 P.M., November 21, a period of one week. Within forty-eight hours it became extremely dilated. There was congestion of the lungs, with expectoration of bloody sputum, the liver became large, tender, and pulsating, and there was deep icterus and edema of the lower extremities. During the first twenty-four hours he was constantly nauseated, but this subsided later. He felt weak and faint, and much of the time was stuporous, with Cheyne-Stokes respiration. All of the usual measures were tried, but without effect on the heart rate, and the patient was *in extremis*.

The medication and state of the heart can best be followed by daily notes:

November 15. Heart rapid (160 to 180) and regular all day.

November 16. 3 c.c. digalen given hypodermically during the day. Heart regular, 160 to 180.

November 17. *At midnight*, 0.5 mg. crystallin strophanthin given intramuscularly. 3 A.M., strophanthin repeated. 5.30 A.M., heart slow and irregular for two minutes. 6.30 to 9.30 A.M., heart slow and irregular, characteristic of auricular fibrillation (Fig. 2). 11.45 A.M., slow and irregular for two minutes. 12.30 P.M., 0.5 mg. crystallin strophanthin given. 10.20 P.M., heart slow and irregular for five minutes. 11 P.M., 0.5 mg., crystallin strophanthin given, a total of 2 mg. in twenty-four hours.

November 18. Continued rapid and regular until 10.30 A.M., when suddenly became slow (90 to 100) and perfectly regular. Great relief and improvement in patient's condition.

November 19. 6.30 A.M., again rapid, regular. 10.30 A.M., 0.5 mg. crystallin strophanthin given. 11 P.M., heart continues rapid, 160. 0.5 mg. crystallin strophthanthin given.

November 20. 10 A.M., rate 144. 1 mg. amorphous strophanthin given. 9 P.M., slow and very irregular for twenty minutes. In auricular fibrillation. 10.30 P.M., rate 164. 1 mg. amorphous strophanthin given.

November 21. 12.20 A.M. to 6.30 A.M., rate 88 to 96 and absolutely irregular. 9.30 A.M., rapid (150 to 160) and regular. 0.75 mg. amorphous strophanthin given. 10.30 A.M., to 1 P.M., slow (82 to 96) and perfectly regular. 7 P.M., rapid since 1 P.M. 1 mg. amorphous strophanthin given. 8.30 P.M., suddenly became slow (76) and perfectly regular. Tracings showed normal curves without evidence of block, alternation of coupling.

November 23. Continued slow and regular until 10.30 P.M., when suddenly became rapid.

November 24. 10.15 A.M., still rapid. 1 mg. amorphous strophanthin given.

11.30 A.M., slow and regular until 3.30 P.M., when became rapid. 9 P.M., rate 170. 1 mg. amorphous strophanthin given.

November 25. 8.30 A.M., continues rapid, regular. 1 mg. amorphous strophanthin given.

November 29. Heart has been slow and perfectly regular until today when it became rapid at 11.40 A.M. 2.30 P.M., 1 mg. amorphous strophanthin given. 3.40 P.M., paroxysm ceased.

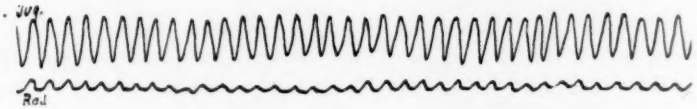

FIG. 1.—Tracing taken during a paroxysm. Pulse rate, 168.

During the next month the heart regained its compensation, though paroxysms recurred every three or four days. Many ceased in an hour or less, but if they lasted more than three hours 1 mg. of amorphous strophanthin was injected into a muscle and

FIG. 2.—Tracing taken November 17, 1911, between paroxysms of regular tachycardia. Rate, 110; auricular fibrillation.

they invariably stopped within three hours and usually in about one hour. The rhythm between attacks was always normal.

From November 29, 1911, to January 20, 1912, strophanthin was administered on thirteen occasions. On the latter date tincture

FIG. 3.—Tracing taken after onset of permanent auricular fibrillation. Rate, 70; taking digitalis. Fig. 3 (original) could not be reproduced and was left out.

of digitalis was ordered and continued, with brief interruptions when there was evidence of poisoning. Thereafter, while there were many brief attacks, none lasted more than two hours until March 16, 1912, when a coryza developed with a temperature of 101°. A paroxysm began at 6 A.M. At 9 A.M. 1 mg. amorphous strophanthin was given and the attack ceased at 10 A.M., and the heart remained slow and regular all day. During the night the

patient was very restless and had several short paroxysms. The heart again became rapid at 7 A.M., and at 10.30 A.M. showed some evidences of dilatation. Strophanthin was then given as usual, and the attack suddenly terminated in one hour.

He was not seen again until the next day, when he said that his heart had been irregular since the cessation of the last attack, and

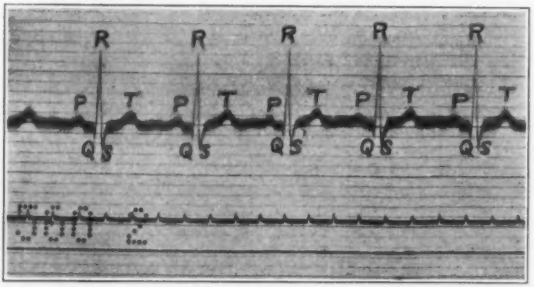

FIG. 4.—Normal electrocardiogram. *P* is due to auricular systole; *Q*, *R*, *S*, *T*, are due to ventricular systole; *P-Q* represents the time consumed in conducting the stimulus from the auricle to the ventricle; *T-P* represents the diastolic period. Time, 0.2 second.

upon examination it showed the characteristics of auricular fibrillation (Fig. 3). This has continued to the present time, and no paroxysms of tachycardia have occurred. While the reserve accommodation force of the heart is slight and there is some pulmonary congestion and a small ascites, the patient is far more comfortable than before and is able to accomplish more work. Digitalis has constantly been necessary, and he is most comfortable

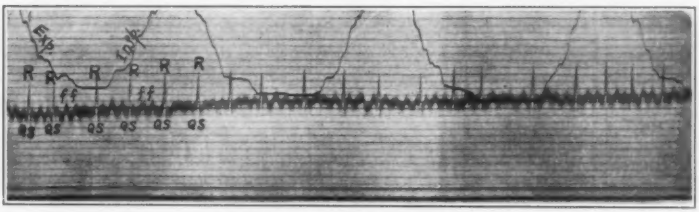

FIG. 5.—Patient's electrocardiogram. Lead II (right arm and left foot). Time, 0.2 second; pulse rate, 108.

when the heart rate is between 60 and 70, a point which I have observed in many instances of auricular fibrillation.

It is unfortunate that no electrocardiograms were obtained from this patient during a paroxysm, but, despite repeated arrangements for them, the attacks never developed at a time and place where they could be taken. However, on April 2, 1912, two weeks

after the onset of permanent auricular fibrillation, electrocardiographs records were taken by Dr. T. Stuart Hart, to whom I am greatly indebted for the ones here reproduced (Fig. 6) and for the interpretation which follows.

(NOTE. A normal electrocardiogram (Fig. 4) is shown to facilitate comparison with that from the case reported.)

The electrocardiograph records of this case (Fig. 5) show the usual features of auricular fibrillation:

1. Complete irregularity: the ventricular complexes are separated by unequal intervals; long and short diastolic periods follow one another haphazard without any rule or fixed relationship.

2. The *P* wave is absent.

3. There is a series of small waves (*ff*) which continue without interruption throughout the whole of the systole and diastole; these are probably due to the fibrillary activity of the auricle, and occur at a rate of about 375 per minute. The ventricular rate is 108 per minute.

This case presents certain special features. The ventricular complexes, of which the *R* waves are the most evident features, are distorted by the coincident occurrence of the fibrillation waves (*ff*). The *R* waves show a considerable variation in size and are influenced by two factors: they are largest at the end of expiration and smallest in the early part of inspiration, and they vary in height according as they occur coincident with a peak of a fibrillary wave or with a depression between the fibrillary waves. The waves *Q* and *S* are fairly well marked. The *T* waves are small, and for the most part so distorted by the simultaneous occurrence of the fibrillary waves that they can be made out only with great difficulty.

The waves of auricular activity (*ff*) are unusually large and fairly rhythmic. If one disregards the distortion caused by the simultaneous occurrence of the *R* waves of ventricular activity the rhythmic character of the fibrillary waves is seen extending over long periods. The rate of these waves is comparatively slow, for one often sees cases of fibrillation with a fibrillary rate between 500 and 600 per minute. These features—(1) the size, (2) the slowness, and (3) the rhythmicity—suggest that the mechanism of this case is one of auricular fibrillation, which is on the borderline not far removed from the cases of auricular flutter, in which are very rapid (up to 300) coördinated contractions of the auricles with a ventricle which responds to every second or third auricular impulse.

Lewis[1] has shown that the mechanism of auricular fibrillation, auricular flutter, and paroxysmal tachycardia is formation of impulses at an abnormal point (heterogenetic impulse formation)

[1] Mechanism of the Heart Beat, London, 1911, pp. 190–193; Heart, 1912–1913, iv, 171.

in the auricular wall. He concludes that in paroxysmal tachycardia the impulses are generated at a single point, while in auricular fibrillation impulses are generated incoördinately in many foci. In auricular flutter also there is, according to Ritchie,[2] "stimulation, excessive in frequency and intensity, of a localized area in some part of the auricular wall." It is, therefore, evident that, so long as the auricle is in fibrillation, paroxysms of regular tachycardia cannot occur. Hewlett[3] and Mackenzie[4] have also reported cases of paroxysmal tachycardia which under digitalis developed auricular fibrillation, sometimes temporary, with cessation of the attacks.

The only drugs of value in auricular fibrillation are the digitalis bodies, and it is in this condition that their best effects are seen. In auricular flutter, also, Lewis[5] and Ritchie[6] recommend digitalis, each reporting instances in which the normal rhythm has been restored by its use. The return to normal rhythm was often preceded by a short period of auricular fibrillation. Inasmuch as the mechanism of paroxysmal tachycardia is somewhat similar to that of auricular fibrillation, and almost exactly like that of auricular flutter, one might well expect benefit from the use of digitalis in regular tachycardia, such as was obtained by the administration of strophanthin in the case here reported.

The pharmacological action of strophanthin is the same as that of digitalis. It has many advantages in an urgent state, such as prolonged tachycardia with a dilating heart, notably ease of administration by intramuscular injection, which insures rapid absorption and, therefore, prompt effect.

Strophanthin is a powerful, and sometimes dangerous, drug, but it should often be repeated more frequently than is usually done, that is, until a satisfactory effect such as is obtained after several days of digitalis administration by mouth is secured. The patient must be watched carefully for indications of severe poisoning, especially a high grade of heart-block, which can be released by atropin. The induction of auricular fibrillation should not be feared, as, when that occurs, the tachycardia will cease, and it may be transitory, the heart subsequently returning to the normal rhythm. Even if it persists it is often a conservative state and reduces the limits of response very slightly.

I have had only one other opportunity to use strophanthin in prolonged and regular tachycardia as most attacks cease spontaneously or are relieved by vagal pressure. This was in a woman, aged forty-three years, who was brought to Bellevue Hospital with bronchopneumonia. She stated that during the previous four

[2] Auricular Flutter, New York, 1914, p. 28.
[3] Jour. Amer. Med. Assoc., 1908, li, 655.
[4] Heart, 1910–1911, iii, 273.
[5] Loc. cit.
[6] Loc. cit.

years she had suffered from frequent attacks of rapid heart action which began and ended abruptly. The present attack, which began shortly after the onset of the pneumonia, had lasted five days. The rate of the heart was about 200 per minute, and it was extremely dilated. Her feet were swollen and the liver was pulsating. She was given an intramuscular injection of 0.5 mg. crystallin strophanthin, and as no effect was noted this was repeated in three hours. Within a half-hour after the second injection auricular fibrillation developed and her distress was greatly relieved. On the next day the edema was lessened and her liver had ceased to pulsate. Auricular fibrillation continued until her death two days later from vasomotor failure and venous stasis did not recur. An autopsy was unobtainable.

SUMMARY. A case of paroxysmal tachycardia with the ventricular form of the venous pulse is reported. Strophanthin was administered many times during the attacks and they always ceased following it,—usually in about one hour. On several occasions transitory fibrillation of the auricle terminated attacks. Finally under the combined effect of digitalis and strophanthin permanent auricular fibrillation was induced and no more paroxysms have occurred. The case illustrates the close relation between paroxysmal tachycardia, auricular fibrillation, and auricular flutter.

Strophanthin, in repeated doses if necessary, is recommended for prolonged attacks of paroxysmal tachycardia.

THE EFFECTS OF EXERCISE ON THE NORMAL AND PATHOLOGICAL HEART; BASED UPON THE STUDY OF ONE HUNDRED CASES.

BY CHARLES SPENCER WILLIAMSON, B.S., M.D.,

PROFESSOR OF MEDICINE AND CLINICAL MEDICINE, COLLEGE OF MEDICINE, UNIVERSITY OF ILLINOIS.

FOR a number of years the question of acute dilatation of the heart has been a debated one. Many attempts have been made to settle the question both by clinical observations and direct experiment, but these have led to no generally accepted conclusions. Until about a decade ago there was practically no difference of opinion on the subject. It was conceded that a normal heart when subjected to even relatively slight strains would dilate to a degree dependent upon the severity of the strain. If the heart were normal this dilatation was relatively soon recovered from—a sort of physiological dilatation. In the event of the heart already being weakened from disease this dilatation might become permanent.

This view of acute dilatation of the heart found its best-known exponent, at least in the German-speaking countries, in the Schotts[1] (Aug. and Theo.). These authors took the view that even relatively slight exercise, such as wrestling moderately or bicycle-riding of moderate rapidity and duration, was quite sufficient to produce a perceptible degree of dilatation in a normal heart. In 1890 Theo. Schott undertook to settle the question in a direct, experimental way. He recognized that in the cases reported clinically as instances of acute dilatation of the heart the heart muscle might not have been quite normal, hence such cases were not altogether free from the possibility of error. Schott, therefore, by the accepted methods of percussion, measured the outlines of the heart before and after exercise in wrestlers, and found that the heart outline actually increased, after only a very few minutes of wrestling, from 1 to 2 cm. in transverse diameter.

With the advent of the Moritz orthodiagraph the question was studied by this author along the same lines as Schott had done using, however, the newly invented instrument to determine the size of the heart. Moritz,[2] using four wrestlers and three bicyclists for his subjects, was unable to determine in them, after even very severe exertions, any dilatations such as Schott had found. At first sight it seemed as if the heart were really smaller after exertion, because the left edge of the heart was farther in; but this he considered to be due rather to a lowered condition of the diaphragm, that is, more of an inspiratory condition, allowing the apex to swing downward and inward. Lennhoff and Levy Dorn[3] carried on a similar series of experiments on wrestlers, but could not determine any trace of dilatation.

Aug. Hoffmann,[4] also using the orthodiagraphic method, came to the conclusion that dilatations of any noticeable degree do not occur in normal hearts. He quotes von Leyden in support of his position, inasmuch as the latter author had held that patients with acute dilatation of any considerable degree had but little prospect of recovery. Mendel and Selig[5] conducted tests on two wrestlers who wrestled to the point of exhaustion. One showed no dilatation and the other even showed a certain degree of contraction. Kienbock, Selig, and Beck[6] carried on investigations on the contestants in swimming matches, and found in 11 cases, 10 instances of acute diminution of the heart.

De la Camp,[7] after a series of experiments on both human beings and animals, came to the same conclusions as did Hoffmann.

[1] Verhandlungen d. IX Kongress f. innere Medizin, 1890.
[2] Münch. med. Woch., 1902 and 1905.
[3] Deut. med. Woch., 1905.
[4] Verhandlungen d. Kongress f. innere Medizin, 1902.
[5] Med. Klinik, 1907 and 1908; Wien. Med. Woch., 1907.
[6] Münch. med. Woch., 1907.
[7] Zeitsft. f. k. Med., 1903–1904, Bd. li.

His experiments embraced both normal and pathological cases, using the orthodiagraphic method to determine the size of the heart. In some normal patients who exercised to their limit of endurance on an ergometer he found only slight changes in the cardiac diameters, the largest (in two cases) being only 0.5 cm. in the sense of an increase. In his experiments on pathological cases he found that slightly weakened patients, such as those suffering from moderate tuberculosis, showed relatively little change after exercise. In a few hearts that were seriously damaged, more marked dilatations occurred. His animal experiments led him to the same conclusions. As a result of both human and animal experimentation, de la Camp concludes that acute dilatation of the heart occurs, even after maximal exertions, only when the integrity of the heart muscle is seriously impaired.

In 1908 Moritz,[8] still using the orthodiagraphic method, had arrived at the conclusion that the heart actually does grow smaller after exercise, and that even the pathologically dilated heart might diminish in size. Moritz even suggests that this latter fact might throw some additional light on the question as to whether hypertrophy or dilatation exists in a given case. On the other hand, Schott,[9] in 1897, repeated his previous experiments with wrestlers and bicyclists, using the roentgen-ray picture to determine the size of the heart, and again came to the conclusion that such exercise produces marked dilatation. Judging from the published report, his roentgen technique, even for that day, was not good, and his cases were too few in number to carry conviction as to the correctness of his results. In 1908 Schott[10] investigated the problem for the third time. In this series of experiments he used the orthodiagraph, and his results substantiated his early findings, for he concluded that "bodily exertion which is carried so far as to produce perceptible palpitation and marked dyspnea leads at last to acute dilatation of the heart."

Hornung,[11] who had opportunities of seeing a large number of cases of heart disease in the Sanitorium Schloss Marbach, examined with the orthodiagraph some 1100 patients in the course of seven years. Hornung was already aware of the occurrence of acute dilatation in the acute infections, since in 1900 he had reported cases in pneumonia. He considers acute dilatation in patients with even slight cardiovascular disorders as much more frequent than has hitherto been thought, and states that he has seen many such cases. According to him, very slight exertions or a temporary sojourn at a high altitude or even fright suffices to produce in those with already damaged hearts, acute dilatation. He considers,

[8] Münch. med. Woch., 1908, No. 14; 1908, No. 25.
[9] Deut. med. Woch., 1897, No. 14; 1897, No. 31.
[10] Münch. med. Woch., 1908.
[11] Berlin. klin. Woch., 1908.

however, that in normal individuals the question of acute dilatation is still (1908) *sub judice*. Hornung's results are directly opposed to those of his co-workers, and constitute virtually a return to the view of von Leyden and his school. Indeed, he goes further than von Leyden or even Schott ever did, in that he finds that in many cases merely psychical traumata can produce acute dilatation.

The opinion of Sir Clifford Allbutt,[12] whose essays on cardiac overstress rank among the earliest and most important contributions to this subject, should be of peculiar value, since in 1909 he writes again (in his *System of Medicine*) an extensive article upon this same theme. He says: "After a period of uncritical appreciation of physical signs, especially by the Nauheim school—and for such disorders as these at any rate over wrought therapeutical schemes—a reaction has set in, which, as is usual in the course of opinion where the facts are intricate, is veering to the opposite extreme. The researches of de la Camp and his colleagues, able and important as they are, carry us too far, if they dictate to us that by no voluntary effort are the dimensions of the heart substantially altered. Are not the orthodiagraphists in their turn assuming a somewhat unreasonable dictation which in the Nauheim school we have deprecated? In their valuable method I am personally unskilled, but my not infrequent opportunities of seeing the work of others convince me that as yet there is almost as much uncertainty in the appreciation of magnitudes by orthodiagraphy as by percussion. Of moving objects its pictures are fugacious and the apparent dimensions are still subject to deceptive space-relations." From this and many other similar passages it is evident that this author declines to accept at par the findings of the various workers with the orthodiagraph, and abides substantially by his early conceptions, albeit with a little more reserve as to the limitations of percussion.

The most recent work on the subject is that of Nicolai[13] and Zuntz, published in May, 1914, at a time when practically all of the actual work of this study had been completed. These authors experimented with normal subjects, causing them to work upon an apparatus (Tretbahn) so constructed as to closely imitate mountain-climbing. They strapped the plate holder to the patient's chest and arranged the apparatus so that, without stopping except for the actual exposure time, the subject could lean against a board, and thus a roentgen-ray picture could be taken actually during the exercise as well as before and after. They found the average transverse diameters to be: At rest, 12.8 cm.; during work, 13.2 cm. (increase 0.4 cm.); after work, 12.0 cm. (decrease 1.2 cm.).

According to these authors the diminution in the size of the

[12] System of Medicine, 1909, vi, 196.
[13] Berlin. klin. Woch., May 14, 1914.

heart occurs suddenly, within three seconds after the cessation of exercise, that is, in one or two beats the heart pumps itself empty. They do not lay special stress on the actual figures given, feeling that the margin of error may be considerable, but qualitatively they regard the result as absolutely correct. They adopted an exposure time of one-half second, in criticism of which it should be noted that with a pulse of about 70, such as would probably obtain with their subjects before the beginning of the exercise, this exposure would not include an entire cardiac cycle, hence in these plates they had no way of telling whether the exposure was taken in systole or diastole. Their pictures were taken with a tube distance of one meter, which is not enough to avoid serious distortion, which they attempt to allow for by calculating the enlargement due to the widely divergent rays, and then making the necessary substraction. Their experiments included only four subjects, all presumably normal.

The interpretation which Nicolai and Zuntz put on their work is that during the exercise the right side of the heart is extra well supplied with blood, owing to the activity of the skeletal muscles, and that to this is due the slight increase in the size during work.

This is not, they think, to be interpreted in any way as a sign of cardiac weakness. They believe that instantly after the cessation of exercise this centripetal flow stops in a large measure, and the volume of the heart then rapidly lessens, owing to the increased output of the heart keeping up for some time.

Because of the divergent conclusions arrived at by the authors above mentioned it seemed desirable that the entire question should be investigated afresh. Our work was begun in December, 1913, and finished in May, 1914.

In view of the rather contradictory findings of the investigators who used the orthodiagraphic method it seemed imperative, in any further research on the subject, to use a more objective method.

After careful consideration we believe that the teleroentgen method offers many unquestioned advantages over all other roentgen procedures, and this was, therefore, selected as the method of choice. The usual manner of taking chest exposures gives a considerable degree of distortion due to the nearness of the tube to the object, so that the latter is unduly magnified. As is well known, this false magnification becomes rapidly less with an increase of distance of the tube from the plate, so that with a distance of 200 cm. or even of 150 cm. it becomes a negligible factor. Schmincke[14] has shown that with the former distance the error in taking the silhouette of the heart is only about 1 mm. in each direction. In our experiments the distance of tube from plate was seven feet one inch (or 216 cm.), so that under the conditions of the

[14] Zentbl. f. Herzkrankheiten, 1911

experiment the enlargement due to this cause certainly does not exceed 1 mm. To all intents and purposes the outlines of the heart obtained by the teleroentgen method, with a tube distance of 216 cm., may be regarded as corresponding accurately with the actual anatomic outline of the organ. The most important problem was to be able to secure the outline of the heart during its diastole. Since tonus is a function of diastole, and since the degree of dilatation of the heart is, in last analysis, a question of its tone, that is, its condition in diastole, it follows that all determinations of the size of the heart should be made during its diastole. Manifestly this is impossible by even the most refined methods of percussion, and is exceedingly difficult with the orthodiagraph.

An important point in any method of determining the size of the heart by any of the various roentgen processes is to make the measurement in each case with the diaphragm in the same position, that is, at the same height. The importance of this will be appreciated when we reflect on the position the apex of the heart assumes in deep inspiration and in deep expiration. When the diaphragm is lowered in inspiration the apex swings downward and inward and the reverse in deep expiration, the apex being raised and pushed outward.

Moritz has called special attention to this movement of the apex and to its effect upon the transverse diameter of the cardiac silhouette. Of two measurements of the same heart under the same condition, one taken with the diaphragm in a position of maximum expiration and the other in a condition of maximum inspiration, the latter will be appreciably smaller, owing to the approximation of the apex to the median line. We have made a number of experiments along this line and find that the apparent difference in size due to different heights of the diaphragm may amount to 20 mm. or even more. *Any method of measurement which does not take the position of the diaphragm into accurate consideration cannot be regarded as satisfactory.* In our experiments maximum inspiration was selected as the phase for taking the exposures, since it is the phase of respiration most easy to determine and reproduce with accuracy. One special advantage of the teleroentgen method as used by us is that the position of the diaphragm can be accurately determined on the plate, and any error due to differences in its height may be readily recognized.

This is, of course, a practical impossibility with the orthodiagraphic method. In our work the time of exposure (two seconds) was so short that an appreciable effect on the size of the heart silhouette from the effect of the inspiratory effort would hardly be possible, and inasmuch as the hearts both before and after exercise were always taken while holding the breath in maximum inspiration, any possible change produced by the inspiratory effort itself would be the same in both instances.

METHOD OF PROCEDURE. The details of the method used by us were as follows: The tube distance remained the same throughout all the experiments, namely, 216 cm. (seven feet one inch). After experimentation upon seven people we decided upon the standing position for taking the pictures. In these cases, which were taken with the patient recumbent, the results were not so satisfactory as regards the control of technique, although the variations in size due to exercise were the same. These seven cases have not been, however, included in the tables. A plate holder was arranged so that it could be adjusted to any height by sliding up and down in a rabbeted frame. The patient was made to stand facing the plate holder and with the arms around the frame, so that the chest was held firmly against the plate holder. The chin rested on the upper edge of the holder. With everything in readiness, the patient having previously been stripped to the waist and the tube having been accurately centred beforehand, the patient was caused to take a deep inspiration, and then, while holding this phase, a two-second exposure was made. After the exercise the second exposure was made in precisely the same way, the apparatus remaining set up, just as it was for the first exposure. The patient remained stripped except for a sheet or a loose coat over the upper part of the body, so that it could be instantly removed and the second exposure made immediately after the cessation of the exercise. In this way we sought to avoid the possibility of overlooking any transient change in the heart's outline.

The Roentgen-ray laboratory is immediately adjacent to the stairs on which the patients were exercised, so that the exposure was usually taken before more than twenty seconds had elapsed after the completion of the exercise. The plates were then developed in the usual way. The exercise chosen for the experiments was stair-climbing. The considerations which led to this choice were the following: In order to make even a rough comparison of the energy put forth by different individuals it is highly important that the work they do should be of a nature to which they are accustomed, since, as is well known, a person doing a new and untried kind of work, for example, running a stationary bicycle, may, and usually does, put forth an amount of effort entirely out of proportion to the work actually accomplished. It is quite imperative that the work done shall be of a familiar nature. Stair-climbing meets these requirements, and has the additional advantage that the work done may be readily calculated in terms of the weight of the patient and the vertical height through which the weight is carried. It was, of course, quite impossible to have all the patients climb at the same rate of speed, but this was attempted, in a rough way, in the case of the normal individuals. The tests were so arranged that the subject ran, two steps at a time, at a dog trot, alternately up and down three long double flights of stairs until

he had gone to the limit of his endurance. After repeated preliminary trials it was found approximately how much a young healthy student could do, and it was demanded of each student that he do at least this and more if possible. In a few instances they gave out from exhaustion before doing the stipulated amount of work, and in practically all cases the subjects declared their inability to do more. A study of the pulse rates alone would suffice to show that the amount of effort put forth was in reality quite great. The fact is not lost sight of that athletes, under the stimulus of competition, may put forth much greater efforts than those in our tests, but such men are already trained in wind and limb and do not represent average conditions or subjects.

In the pathological cases the patient was caused to climb the largest number of stairs which seemed safe in his particular case, and at as rapid a rate as he could. In spite of watchful care several patients went beyond their limit and partial syncope developed. In these cases also it is believed that the work done represents about the maximum effort which the patient was capable of putting forth under any ordinary conditions of experiments.

Comparison of the Teleroentgen and Orthodiagraphic Methods. It may be freely granted that theoretically the orthodiagraphic method gives ideal results, but in spite of its theroretical superiority this procedure has serious drawbacks. The first of these is a considerable degree of subjectivity in the interpretation of the findings. Having to work in the dark, with considerable rapidity, on hearts beating at a rate of perhaps 140 to 170 per minute, it is easily comprehensible that, even to the expert, the results cannot always be satisfactory. When we further reflect that the patient after exercise is dyspneic and that the respiratory movements of the diaphragm are necessarily very rapid, it will be seen that this introduces a source of error almost impossible of elimination, since it would be extremely difficult for the patient to hold his breath at any phase of respiration for a sufficient time to permit of the outline to be marked in with a satisfactory degree of accuracy. Perhaps the most serious defect is this inability to be sure as to the position of the diaphragm for any given outline. It is possible that the somewhat greater length of time necessary to outline the heart with the orthodiagraph might be sufficient to allow any evanescent dilatation or contraction to escape. In this respect the method we have employed is vastly superior. A further difficulty with the orthodiagraphic method is that of always obtaining the outline during the same phase of the cardiac cycle, for example, during the diastole. If we consider the diminution in the transverse diameter during systole to amount to 0.5 cm., it will be seen that there is here the possibility of error to that extent. With the method we have employed this possibility of error is eliminated. A little reflection will show that

since, for our purpose, the diastolic outline is desired, that is, the maximum size of the heart, all that is necessary is to be sure that the time of exposure is sufficiently long to include at least one complete cardiac cycle. A two-second exposure time is sufficiently long, assuming even such a slow pulse rate as sixty per minute, to include at least two cardiac cycles, and with the fast pulse rates which obtain after exercise, for example, from 120 to 180, correspondingly more.

The diastolic outline is, therefore, the one obtained under such conditions. As a matter of fact, a double contour was never obtained, since the larger shadow completely encompasses the smaller. One objection which has been raised to the teleroentgen method is that the contours are not so sharp as they might be. Except in the case of exceedingly obese patients this has not proved to be the case, and in such patients it is equally difficult to obtain satisfactory outlines with the orthodiagraphic method. The right border, owing to its smaller range of movement and proximity to the chest wall, is, as a matter of course, always a little sharper and better defined than the rest, as has been found by nearly all observers. In a few cases, owing to extreme obesity or to some movement of the patient or to an imperfect plate, the outlines were not sufficiently clear, and such plates have been of course discarded.

In all our experiments the exercise and second plate were taken immediately after the first, so as to eliminate any possible error due to a different position of the diaphragm, and, therefore, the heart, consequent upon such condition as overfilled stomach, meteorism, etc.

The measurement of the heart's outline was taken in the manner generally recognized as the most reliable. With the plate in the shadow box the median line was drawn in with a T-square, the greatest distance of the heart's outline to the right and left of this median line noted, and the two measurements taken with an accurate millimeter rule. The sum of the two measurements is that given as the transverse diameter.

Classification of Patients. The grouping of the patients was done entirely on the basis of the ordinary methods of examination. For normal subjects, assistants and students were taken who had always been healthy and who were accustomed to engage in ordinary athletics, but no effort was made to pick men of unusual strength or athletic tendencies. In this group also were included patients with minor ailments who were otherwise in good physical condition and in whom the hearts were normal.

The second group consisted of patients with heart lesions in perfect compensation or patients in whom the ordinary examination disclosed no cardiac abnormality, but in whom it was fair to assume some degree of myocardial weakness as a result of severe anemia or

cachexia. The moderately advanced tuberculous cases, nephritis, etc., were also included in this group.

The third group consisted of cardiac cases with frank, but low to moderate grade decompensation, presenting such symptoms as dyspnea on slight exertion, with enlarged and tender liver, edema of the ankles, etc.

In all 125 cases were studied, but 25, for various shortcomings of the negative, such as variable height of the diaphragm, falling of the right cardiac border in the vertebral shadow, etc., were rejected. The results obtained in the remaining 100 cases are given in the following summaries. (N. B.—The detailed results, arranged in tabular form, are omitted here for lack of space, but will be found in full in the reprints.)

GROUP I: SUMMARY.

Total number of subjects	38
Heart contracted	29
Heart dilated	3
Heart remained of same size	1

Maximum contraction, 23 mm.; average, 6 mm.
Maximum dilatation, 1 mm.; average, 1 mm.

In 29 of 33 cases exercise induced definite contraction of the heart, averaging 6 mm., and in 1 case a young, strong athlete, this contraction reached 23 mm. In only 1 case was the heart unchanged in size, and in only 3 did dilatation occur, and then only 1 mm. It is sufficiently obvious that these last figures are within the limits of error of the method of measurement employed. We may conclude, therefore, *that the normal heart responds to any exercise within its power by contraction.*

GROUP II: SUMMARY.

Total number of subjects	57
Heart contracted	24
Heart dilated	25
Heart remained of same size	8

Maximum contraction, 14 mm.; average, 4 mm.
Maximum dilatation, 13 mm.; average, 3 mm.

It is evident that a considerable number of pathological cases with damaged hearts respond to exercise in the same manner as the normal heart, that is, by contraction. Of 57 cases, 24 contracted and 8 remained of the same size. On the other hand, about the same number, 25, dilated.

The average contraction was 4 mm., the average dilatation 3 mm. The maximum contraction was 14 mm., the maximum dilatation 13 mm. The relatively insignificant average amount of dilatation, 3 mm., is especially noteworthy. A perusal of the results shows that many hearts, with apparently normal findings,

in patients with various diseases, dilate after exercise, indicating their lessened tonicity.

GROUP III: SUMMARY.

Total number of subjects	10
Heart contracted in	6
Heart dilated in	4

Maximum contraction, 4 mm.; average, 2 mm.
Maximum dilatation, 4 mm.; average, 3 mm.

A study of the results obtained from the patients in the above group, all of them with manifest broken compensation, indicates clearly that there is a distinct tendency to contraction, this occurring in 6 out of 10 cases. The average degree of contraction, as would be expected, was small, 2 mm. On the other hand, in the 4 cases which dilated the average amount was only 3 mm.

Even to one thoroughly familiar with the reaction of the normal heart to exercise the results obtained in Group 3 is more or less of a surprise, since these show in the most striking way the extreme reluctance of the heart to dilate, even when there is already some degree of myocardial insufficiency present.

VALUE OF THE RESULTS FROM THE STAND-POINT OF FUNCTIONAL TESTING OF THE HEART. The writer has elsewhere[15] laid stress upon the value of exercise tests of the heart as supplemental to the routine examination. From these results it seems clear that a heart which dilates under exercise, which should be within its power, is certainly, functionally speaking, below normal. *Vice versa*, a heart, if normal, should contract promptly and definitely to exercise, so proportioned as to be well within its power. To attempt to draw numerical comparisons would be to exceed the limits of justifiable deduction.

Our results justify the statement that, in cases where the condition of the cardiac muscle is doubtful, considerable light may be shed upon its functional efficiency by correctly taken teleroentgen pictures before and after exercise. Bearing in mind the comparatively slight changes in size which occur, the most scrupulous care must be taken to see that the diaphragm height is the same in both negatives, as any material variation in this respect will cause an error so great as to completely vitiate the results.

CONCLUSIONS. 1. Owing to the great apparent variation in the size of the heart due to different heights of the diaphragm, any method which does not enable us to fix its exact position, and thus to be sure that its height before and after exercise is the same, is valueless.

2. The teleroentgen method, as employed by us, offers a highly accurate and perfectly objective method of determining the size of the heart, eliminating completely any possible error due to varying heights of the diaphragm.

[15] The Functional Testing of the Cardiac Powers, Lancet Clinic, 1914.

3. The results of our experiments show that: (*a*) The normal heart responds to any exercise within its power by a diminution in size; (*b*) About one-half of the pathological hearts, which are in good compensation, respond to exercise within their power, with a diminution in size; (*c*) Approximately one-half of the pathological hearts, with manifest, but low-grade broken compensation, respond in the same manner by some degree of diminution in size.

4. In only the most exceptional instances, if ever, are the differences in size due to acute dilatation, sufficient to be determined by even the most refined and subtle percussion.

5. The Roentgen-ray examination of the heart, before and after appropriate exercise, using the technique employed in this research, is capable of rendering valuable assistance in the estimation of the functional efficiency of the heart.

My sincere thanks are due to Dr. Adolph Hartung, instructor in roentgenology, College of Medicine, University of Illinois, for his generous assistance. The negatives of all the cases were made by Dr. Hartung, and to his skill and coöperation much credit is due.

My thanks are also due to Dr. Ernest S. Moore and Dr. Robert Mosser, instructors in the medical clinic, for assistance in the selection and observation of the cases.

DILATATION OF THE ARCH OF THE AORTA IN CHRONIC NEPHRITIS WITH HYPERTENSION.

By William H. Smith, M.D.,

and

Alson R. Kilgore, M.D.,

Boston, Massachusetts.

(From the West Medical Service of the Massachusetts General Hospital.)

This report is based on Roentgen-ray plates taken in the routine of clinical work at the Massachusetts General Hospital during the last eighteen months by Dr. Walter J. Dodd and Dr. George W. Holmes, to whom we are indebted for permission to use the records of the department. All the plates were taken at a distance of seven feet, that is, with practically parallel rays, thus allowing for quite accurate measurements of the shadows of the heart and great vessels.

With a series of about sixty normal plates available it is not practical to lay down accurate normal limits for the measurements of the transverse diameter of the great vessels, since many of the

plates are slightly distorted on account of not being taken accurately in the frontal plane, etc. The limits of 4.5 and 5.5 cm., however, include by far the largest number of normal measurements (see curve *a*, Fig. 1, of normals). It is fair to state that in no case did the great vessels measure more than 6 cm. in diameter in which there was not evidence of one of the following:

1. Syphilis (*i. e.*, aortitis).
2. Age over fifty years (*i. e.*, probable factor of arteriosclerosis).

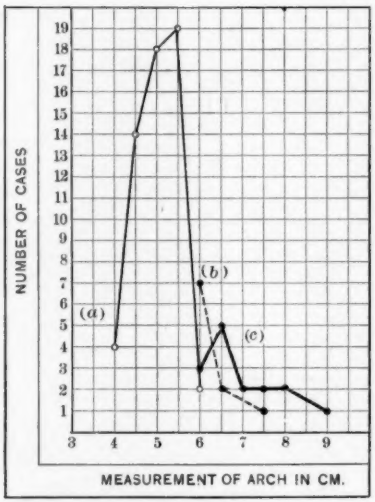

FIG. 1.—To show graphically the limits of arch diameters found in the conditions studied, obtained by plotting the number of cases found at each diameter and including all the cases which had had plates taken at seven feet without selection. *a*, ○——○——○ normal; *b*, ●---●---● cardiac disease with enlargement but without hypertension or syphilis; *c*, ●—●—● chronic nephritis with hypertension.

3. Other serious cardiac disease (*e. g.*, endocarditis or pericarditis with cardiac enlargement).
4. Hypertension (with more or less hypertrophy, *e. g.*, in chronic nephritis).

Therefore, great vessels measuring more than 6 cm. in diameter may usually be considered as dilated.

In this series, cases in which an increase in the diameter of the great vessels could be explained by either (1) syphilis or (2) arteriosclerosis of age have been ruled out, but it is striking to note how many cases of dilated arch remain to be classified under (3) cardiac disease with enlargement and (4) hypertension.

A. Dilatation of the Arch with Other Cardiac Disease.[1] There were ten cases with arches at the upper limit of normal or above (see curve *b*, Fig. 1), in which neither age, syphilis, nor hypertension could be found to explain the dilatation. (As an approximate index of the degree of cardiac enlargement the total transverse diameter of the heart is also given in Table I, *i. e.*, the distance of the right border from the median line plus the distance of the left border from the median line. The maximum normal total transverse diameter of the adult heart is given as 13.2 cm.[2]).

Table I.—Cases of Dilatation of Arch Associated with Other Cardiac Disorders.

Case.	Age.	Diameter of arch.	Total transverse diameter of heart.	Blood-pressure.	Diagnosis.
		Cm.	Cm.		
1	36	6.0	14.0	110	Chronic mitral endocarditis.
2	41	6.0	18.0	110	Chronic mitral endocarditis.
3	28	6.0	15.0	100	Chronic mitral endocarditis.
4	18	6.0	14.0	140	Chronic aortic endocarditis.
5	40	6.0	14.5	120	Hyperthyroidism with hypertrophy.
6	27	6.0	16.0	110	Chronic aortic and mitral endocarditis.
7	24	6.0	12.0	130	Chronic aortic and mitral endocarditis.
8	25	6.5	18.5	120	Chronic aortic and mitral endocarditis.
9	33	6.5	19.0	110	Pericarditis.
10	43	7.5	15.5	100	Adherent pericardium.

All of these cases, therefore, had some other definite cardiac lesion, and most of them had considerable increase in the heart size. Whether the measurements of the Roentgenograms represent the actual degree of dilatation of the arch, or whether some of the increase in diameter may be explained by distortion brought about by the cardiac enlargement, is a question which must be settled by autopsies, by Roentgen rays taken in several planes, etc. The point brought out is that many cases of cardiac disease without syphilis or hypertension show by Roentgen rays, great vessels whose diameter is at the upper limit of normal (6 cm.) or above.

B. Dilatation of the Arch with Hypertension. There were fourteen cases of chronic nephritis in which chest plates had been taken at a distance of seven feet. The blood-pressures ranged from 185 (one case) to 270, taking in each case the highest blood-pressure recorded while in the hospital. The average was 215. The ages were from 29 to 54, averaging 43. The transverse diameters

[1] A well-recognized condition; see McCrae, Dilatation of the Aorta, Amer. Jour. Med. Sci., 1910, cxl, 469.

[2] Groedel, Die Rontgendiagnostik der Herz- und Gefässerkrankungen, Berlin, 1912.

of the hearts varied from 13.5 (one case) to 19 cm., averaging 16 cm. (normal maximum 13.2 cm.).

All but three of these cases had great vessels whose transverse diameters measured over the normal limit of 6 cm., and in one of those measuring 6 cm. the Roentgen-ray diagnosis was "slight dilatation of the arch." In two cases the diameter was 7 cm.; in two cases 7.5 cm.; in two cases 8 cm.; and in one case 9 cm. (See curve *c*, Fig. 1, cases of chronic nephritis.)

TABLE II.—Cases Showing Dilatation of Arch with Chronic Nephritis and Hypertension.

Case.	Blood-pressure.	Diameter of arch.	Transverse diameter of heart.	Age.	Wassermann.
		Cm.	Cm.		
1	240	6.0	16.5	53	Negative.
2	190	6.0	16.5	38	Negative.
3	200	6.0	14.5	49	Negative.
4	230	6.5	14.0	54	Not done.
5	190	6.5	16.0	38	Negative.
6	270	6.5	17.5	45	Negative.
7	200	6.5	15.5	42	Negative.
8	220	7.0	13.5	35	Negative.
9	220	7.0	15.0	35	Negative.
10	185	7.5	18.0	29	Negative.
11	220	7.5	15.0	43	Negative.
12	190	8.0	19.0	43	Negative.
13	250	8.0	14.0	50	Negative.
14	220	9.0	18.5	48	Negative.

In the production of the varying degrees of dilatation of the arch in chronic nephritis four factors must be considered:

1. *Cardiac Hypertrophy*, since it has been shown above (see curve *b*) that (apparent) dilatation of the arch occurs in association with simple cardiac enlargement without hypertension. The diameter of the heart in each case has been plotted as a curve (*d*, Fig. 2), which shows a general but by no means constant increase of the size of the heart with the size of the arch. It will be noted, however, that the degree of dilatation occurring in chronic nephritis is much more than that found associated with simple hypertrophy (curve *c*), so that another factor must evidently be found.

2. *Hypertension* is an obvious factor. The degree of hypertension in each case when plotted as a curve, however (curve *e*, Fig. 2), does not show the greatest hypertensions to be associated constantly with the greatest degrees of dilatation.

3. *Duration of the Hypertension* is undoubtedly an important factor. Chronic nephritis, however, being a disease of notoriously insidious onset, it is almost impossible to determine accurately the duration of any given case from a hospital record, and it was found in this series that no constant relation could be demonstrated between the apparent duration and the size of the arch or

the size of the heart. It is probable that the degree of dilatation of the arch is related to all three factors: the degree and the duration of hypertension and to a small extent associated with the simple cardiac enlargement.

4. *Age.* It was found that the average age of the cases of chronic nephritis with arches measuring from 6 to 7 cm. was 45.5, while the average age of those measuring from 7 to 9 cm. was 40.4. This is contrary to what would be naturally expected, since dilatation of the arch is common, associated solely with the arteriosclerosis of age. It has been suggested as a tentative explanation

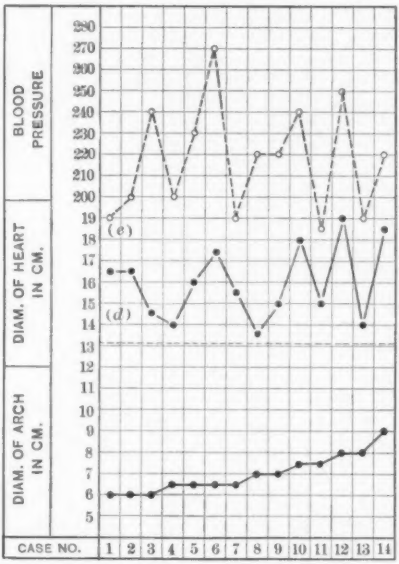

FIG. 2.—Blood-pressure and size of heart in each case of chronic nephritis, arranged in order of increasing diameters of arches. *d*, ●——●——● diameter of heart; *e*, ○---○---○ blood-pressure.

that when hypertension supervenes on an aorta already somewhat stiffened from age it does not stretch as easily as does a young one.

CONCLUSIONS. The point of interest brought out by these cases is the frequency of dilatation of the arch under the age of fifty years in non-syphilitic conditions, especially in chronic nephritis with hypertension. In such cases there were no aortas below the upper limit of normal diameter (6 cm.); three aortas at the upper limit of normal; and eleven aortas definitely dilated. This dilatation may be quite marked—especially in the younger patients—in seven, or 50 per cent., of these cases the diameter measured from 7 to 9 cm., or 1 to 3 cm. above normal.

ACRODERMATITIS CHRONICA ATROPHICANS: ITS SYMPTOMATOLOGY AND DIAGNOSIS.

By Fred Wise, M.D.,
AND
E. J. Snyder, M.D.,
OF NEW YORK.

(From the Dermatological Department of the College of Physicians and Surgeons, Columbia University, New York.)

Although the literature on the subject of acrodermatitis chronica atrophicans is already voluminous and quite comprehensive, more especially in the German language, still the incidence of a case of this type of atrophy of the skin nearly always kindles the interest of him who observes it; besides, rarely is a case presented before a body of dermatologists without exciting more or less controversial discussion as to the nosological position of the disorder. This statement applies chiefly to American dermatologists, for our European confrères seem to have the relationship between this and other types of atrophies pretty well fixed in their minds.

In a previous essay[1] we presented a clinical and histological study of a case of acrodermatitis chronica atrophicans occurring in a woman, aged fifty-eight years, who, aside from her cutaneous disorder, appeared to enjoy normal health. This case (Mrs. B. D.) was peculiar in that it presented an unusual abundance of the soft, doughy, tumor-like masses to which Herxheimer[2] called attention in his second paper on the subject, published in 1905. We attempted to show, in the article dealing with the above-mentioned case, that the clinical features of the dermatosis were sufficiently well-marked and characteristic to uphold the contentions of Herxheimer and Hartmann,[3] who differentiated this form of diffuse idiopathic atrophy of the skin from the clinical types akin to it.

Soon after the publication of this report a second case of the same malady came under the observation of Dr. MacKee and ourselves in the dermatological department of the Vanderbilt clinic. The remarkable and extensive changes which the skin of these patients exhibit, coupled with an etiology as yet shrouded in utter obscurity, incite us to record an additional case in the literature.

[1] Wise, Fred., Acrodermatitis Chronica Atrophicans; the Transition from Infiltration to Atrophy, Jour. Cutan. Dis., April, 1914, xxxii, No. 2.

[2] Further Observations on Acrodermatitis Chronica Atrophicans, Jour. Cutan. Dis., 1905, xxiii, p. 241.

[3] Ueber Acrodermatitis Chronica Atrophicans, Arch. f. Dermat., 1902, lxi, pp. 57 and 255.

The idiopathic progressive atrophies of the skin, while resembling each other in their clinical and histological aspects, have certain distinctive characters for each type. Although it is true that these characters may not always be easily differentiated, inasmuch as one type may appear to merge into another, or two or more types may occur together, it is also true that careful clinical observation and study will reveal certain differences which, though sometimes vague, are at other times quite patent, in various types of cutaneous atrophies which at first glance seem to be almost identical in course, appearance, and evolution.

Finger and Oppenheim,[4] in 1910, published a complete monograph on the subject of the cutaneous atrophies, in which they described, more or less exhaustively, most of the dermatoses in which atrophy plays a part as an essential symptom.

They divided the subject into two main groups, which, for the sake of better orientation, we will note here. The first group comprised all those cutaneous atrophies which are to be differentiated from the true progressive, chronic, atrophying dermatitides, and included:

1. Congenital atrophies.
2. Striæ and maculæ distensiæ.
3. Cutaneous atrophies following nerve lesions.
4. Cutaneous atrophies following chronic infectious diseases of the skin.
5. Senile atrophy and atrophy due to exposure to heat, cold, winds, etc. (element atrophy).
6. Xeroderma pigmentosum, blepharochalasis, kraurosis vulvæ.

The second large group included the idiopathic atrophying dermatitides, with the following sub-groups:

1. Dermatitis atrophicans progressiva idiopathica chronica diffusa.
2. Acrodermatitis chronica atrophicans.
3. Dermatitis atrophicans maculosa.
4. Combinations of dermatitis and acrodermatitis atrophicans chronica idiopathica diffusa, with dermatitis atrophicans maculosa.

It is with the second of these sub-groups, acrodermatitis chronica atrophicans, that this paper is concerned. This type of diffuse progressive atrophy of the skin was first described by Herxheimer and Hartmann[5] in 1902. It is an inflammatory disease, usually beginning on the backs of the fingers and the feet, progressing very slowly and insidiously upward; the inflammation gradually gives place to infiltration and tumor formation, which, in turn, is succeeded by the characteristic atrophy. In addition to the terminal atrophy there may also appear one or more hard, fibrous

[4] Die Hautatrophien, F. Deuticke, Wien und Berlin, 1910, containing most of the literature to date.

[5] Loc. cit.

nodules—"end products" of the disease—usually occurring in the vicinity of the knees and elbows. Pigmentations and depigmentations, telangiectases, desquamation, cutaneous hemorrhages, etc., also play a part in the symptom-complex. The disease is very chronic in its course, and is usually free from subjective symptoms.

The chief diagnostic points to be considered in acrodermatitis chronica atrophicans are the following:

1. The morbid changes usually begin on the backs of the hands and feet and slowly advance upward toward the knees and elbows in a centripetal manner. Hence the name "acrodermatitis," from the Greek "acra," extremity.

2. They are accompanied by well-marked inflammatory and infiltrative formations, which culminate in atrophy. This atrophy is of the peculiar "wrinkled cigarette-paper" type, to which Jadassohn[6] applied the term "anetodermie." The skin appears transparent, loose, wrinkled into fine parallel folds, has lost its elasticity, and can be easily raised from the underlying tissues. It has a silky or velvety feel. The color is rose red or bluish red. The subcutaneous fatty tissue is absent. The underlying veins and tendons shine through the translucent skin.

3. The occurrence of the so-called "ulnar band," to which Herxheimer[7] first called attention. It consists of a strip of inflamed skin, running up the forearm from the wrist to the elbow, usually overlying the ulnar bone. An analogous band may appear on the leg. It occurs as a more or less circumscribed, edematous, or infiltrated band of inflamed skin, varying in length and breadth. In consistency it may be soft and doughy or hard and resistant. The color may be a bright or a dusky red or it may be violaceous. The surface may be tense or wrinkled. It is present during the stage of infiltration and later gives place to the characteristic atrophy. This ulnar band seems to be peculiar to acrodermatitis chronica atrophicans. It is present in the patient who forms the subject of this report, and was described in the case reports of Herxheimer and Hartmann,[8] Bruhns,[9] Lehmann,[10] Baum,[11] Leven,[12] Rusch,[13] Hertmanni,[14] Finger and Oppenheim,[15] Neumann,[16] and others.

4. In the majority of cases of acrodermatitis chronica atrophicans there appears to be an area of skin which seems to be almost

[6] Atrophia maculosa Cutis, Zweiter Kong. Deutsch. dermat. Ges., 1891.
[7] Loc. cit. [8] Loc. cit.
[9] Ueber idiopathische Hautatrophie, Charité Annalen, 1901, xxv.
[10] Ibid., Inaug. Diss., Leipzig, 1902.
[11] Acrodermatitis Chronica Atrophicans, Arch. f. Dermat., 1903, lxiv, p. 446.
[12] Ibid., 1903, lxv, p. 247.
[13] Ueber idiopathische Hautatrophie und Sclerodermie, Dermat. Zeitsch., 1906 xiii, p. 749.
[14] Verh. X Kong. Deutsch. dermat. Ges., 1908, p. 290. [15] Loc. cit.
[16] Lehrbuch der Hautkrankheiten, 1880, 5th ed.

immune from the advances of the malady. It consists, roughly speaking, of a triangle of the integument surrounding the genitals, bounded above by Poupart's ligament and at the sides by the anterior and inner aspects of the upper third of the thighs. Such an area of non-affected skin is illustrated in the photograph accompanying our paper.[17]

These four diagnostic points are by no means constant factors in the symptomatology of the disease; indeed, they rarely occur simultaneously in the same patient. The morbid changes which the integument undergoes are manifested by a slow, but nevertheless constant and progressive alteration in the disease picture; these changes begin with an edema and inflammation, after which follow the infiltration and the terminal atrophy. Each of the various pathological phases of the disease—inflammation, infiltration, atrophy—may involve a period of months or years in their evolution and development. It must be borne in mind that patients have presented themselves for treatment or observation in whom the disease has existed anywhere from a few weeks (Herxheimer and Hartmann) to a great many years (forty years in Wise's case). It is evident, therefore, that a given case may present only one or two of the characteristic points mentioned above, the other features having long since disappeared. The peculiar "ulnar band," for example, may persist for a certain number of weeks, months, or even years without ever having come under the physician's observation. Many of the reported cases have presented themselves long after the subsidence of the active morbid changes, and in whom the terminal atrophy and anetodermia are the only characteristic remaining features of the dermatosis.

On the other hand it may be well-nigh impossible for the most astute diagnostician to recognize the malady in its earlier stages. A chronic edema and inflammation of the backs of the hands, or of the feet, persisting for a number of months without subjective disturbances, may be interpreted in a number of different ways; not until the advent of infiltrative lesions, accompanied by or culminating in atrophy of the affected integument, is there a likelihood that the true nature of the disease would be recognized. Thus, Ehrmann[18] and Weidenfeld[19] have reported instances in which the disease was ushered in by acute swelling and inflammation of the integument, resembling lymphangitis and erysipelas.

It follows, therefore, that in order to formulate a rational symptom-complex of acrodermatitis chronica atrophicans it is necessary to study and compare a number of cases presenting the various evolutionary phases or cycles of the disease, its localization, areas of predilection, mode of progression and termination.

[17] Jour. Cutan. Dis., April, 1914.
[18] Ausgedehnte idiopathische Hautatrophie, Wien. klin. Woch., 1909.
[19] Atrophia cutis idiopathica, Wien. dermat. Ges., November, 1909.

Shortly after the completion of our studies of the case of Mrs. B. D. (*loc. cit.*) there appeared at Professor Fordyce's clinic a second case (Mrs. H. L.) of acrodermatitis chronica atrophicans, also in a middle-aged woman. This patient was presented by Dr. MacKee before the New York Dermatological Society at its October, 1913, meeting.[20] A brief report of the case was subsequently published.[21] The preliminary routine examination of this patient disclosed the interesting fact that her blood showed a positive Wassermann reaction and that a marked glycosuria was present. She had, however, neither cutaneous nor visceral symptoms referable to either syphilis or diabetes at the time she came under our observation.

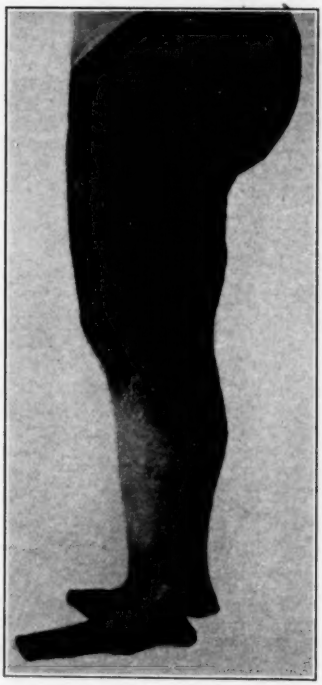

FIG. 1. — Showing anetodermia of thighs and knees, scleroderma-like appearance of legs and ulceration around ankles. (Patient, Mrs. H. L.)

The marked resemblance in the appearance of this patient to that of our first case was striking: the clinical picture which her skin presented possessed so many points of similarity to that of our first patient that one might be almost justified in saying that the one description may apply to both cases if we except the tumor-like, infiltrative masses which appeared on the thighs of our first patient. In addition, however, the second patient interested us on account of the presence of the "ulnar band," mentioned above as being one of the characteristic features of the dermatosis from which she was suffering.

CASE.—Mrs. H. L., aged fifty-four years; married at nineteen. She was born in Stockholm and came to this country when twenty-five. Her family history was negative. She was the only member of the family afflicted with a skin disease.

Personal History. Her first child was born within a year after marriage. Then followed five successive normal pregnancies; of these, two resulted in the birth of healthy children, while three child-

[20] MacKee, Case Demonstration for Dr. Fordyce, Jour. Cutan. Dis., February, 1914, xxxii, No. 2, p. 143.

[21] Jour. Cutan Dis., February, 1914.

ren were said to have died at birth; the cause of the deaths was not ascertainable. She had had no miscarriages. Three of her offspring are living and said to be healthy. The husband is living and apparently in normal health. Twenty years ago she had an attack of gall-stone colic, accompanied by severe gastro-intestinal disturbances. Fourteen years ago she was treated for a severe attack of jaundice at the Long Island College Hospital. No operation was performed. A little over two years ago she had an attack of pneumonia; since that time she has been afflicted with periodic

FIG. 2.—Showing "immune area" below Poupart's ligament; anetodermia of knees and thighs. (Patient, Mrs. H. L.)

attacks of asthma, bronchitis, and articular rheumatism. Shortly after her recovery from pneumonia examination of the urine revealed the presence of glycosuria. Menstruation ceased at the age of forty-eight.

Physical Examination. The patient is a tall, heavy-framed, obese woman, weighing over 200 pounds. Examination of the thoracic viscera (performed by Dr. Kent) revealed the presence of a rather severe bronchitis and asthma. The abdominal viscera were impalpable, due to the woman's obesity. The blood picture

was normal. The Wassermann test (performed by Dr. Jagle) was positive. The urine, examined on several occasions, presented varying small quantities of albumin and sugar. The patient has a florid complexion and her general health is fair. The hair, teeth, and nails are normal.

The cutaneous changes began about twelve years ago. They were ushered in by the appearance of reddened, inflamed, and edematous, slightly elevated, circular and oval patches of skin over the dorsal surfaces of the feet and on the anterior portions of the lower half of the legs, just above the ankles. There was a moderate amount of scaling. Itching was slight. Similar inflamed areas soon made their appearance on the upper half of the legs and on the thighs; these gradually coalesced and spread upward, toward the groins and buttocks, until practically the entire integument of both lower extremities and buttocks was involved in the process. These areas of inflammation, therefore, began to appear at the distal portions of the extremities and, by their coalescence, spread centripetally toward the trunk. The process seemed to be arrested a few inches below Poupart's ligament, anteriorly, thus leaving a triangular portion of the upper and inner aspects of the thighs free of the disease. After persisting, for an indefinite number of months, in the form of red, swollen, and inflamed patches, these areas would assume a purplish or violaceous hue, becoming more or less resistant to the touch, and somewhat elevated above the as yet unchanged surrounding integument. By the time that fusion of the patches had occurred the affected skin had assumed a dark-red, purplish hue, had become glossy, parchment-like, wrinkled, and dry, especially around the knees and ankles. After a lapse of two or three years (the patient's narrative was very indefinite), the skin around the ankles and

FIG. 3.—Showing anetodermia of thighs and buttocks and tense sclerodermia-like skin of legs. (Patient, Mrs. H. L.)

over the shins changed to a yellowish tint and became hardened and bound down over the underlying tissues, while the skin around the knees, on the contrary, became loose, folded, and flaccid. At the same time the superficial veins and tendons began to shine through the skin. Around the knee-joints, on the calves of the legs and on the thighs and buttocks, the skin became at first reddish pink, then darker red, finally assuming a purplish and violaceous hue; this discoloration and accompanying change in

FIG. 4.—Showing the "ulnar band" of right forearm; atrophy of the skin of the hands. (Patient, Mrs. H. L.)

the texture of the skin gradually extended upward until it reached nearly to the waist line at the sides and on the back. About two years ago an ill-defined patch of inflammatory redness made its appearance on the dorsum of the right hand, followed soon after by a similar patch on the left hand. Since then the same changes appeared on the ulnar aspect of the right forearm, running toward the elbow in the shape of a wide band or strip. This ulnar band seems to have developed during the last few months. On the lower extremities the process appears to have come to a standstill. Now

and then small ulcers would appear on the legs and feet as a result of scratching and infection. The pruritus has always been moderate in severity.

Examination. The affected portions of the integument were distinctly atrophic. The appearance, however, of the various areas of atrophic skin was by no means a uniform one. On the dorsum of the feet, around the ankles and over the tibiæ, the skin was waxy, glistening, smooth, yellowish, and "bound down" over the underlying tissues. To the touch it was hard and resistant, resembling the condition seen in ordinary sclerodermia. Over the

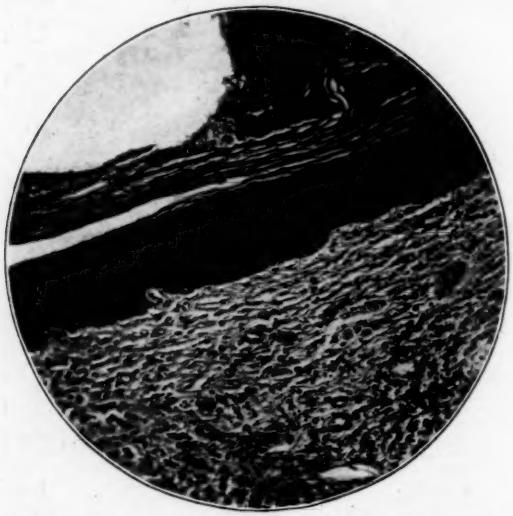

FIG. 5.—Showing hyperkeratosis, loss of interpapillary pegs, absence of papillæ, edema of collagen, lymphocytic infiltration of the corium.

calves of the legs, on the thighs and buttocks, and in the popliteal spaces the integument was thin, more or less wrinkled, flaccid, reddish pink in color and transparent, permitting the underlying veins to shine through as tortuous, blue strands, varying in width and in prominence. Around the knee-joints the skin seemed to be redundant, hanging in loose folds with the patient in the erect position; the surface showed a fine, parallel wrinkling, giving to it a characteristic silky appearance; the color was rose red; to the palpating finger the skin gave a velvety impression, as though it were loosely distended with air or water. When a fold was lifted between the fingers and then released an utter lack of resiliency was manifested. The entire integument of the lower extremities and the buttocks was implicated in this atrophic process, with

the exception of a small triangular area on the inner aspect of the thighs, just below the groins. The upper limiting border of the process showed a somewhat abrupt line of demarcation.

On the buttocks and on the anterior and posterior surfaces of the thighs there were twenty-five to thirty small, rounded, slightly elevated subcutaneous nodules, varying in size from a lentil to that of a pea. They were barely visible, their color differing but little from that of the surrounding integument; but on palpation they could be made out without difficulty, on account of their fleshy, semisolid consistence.

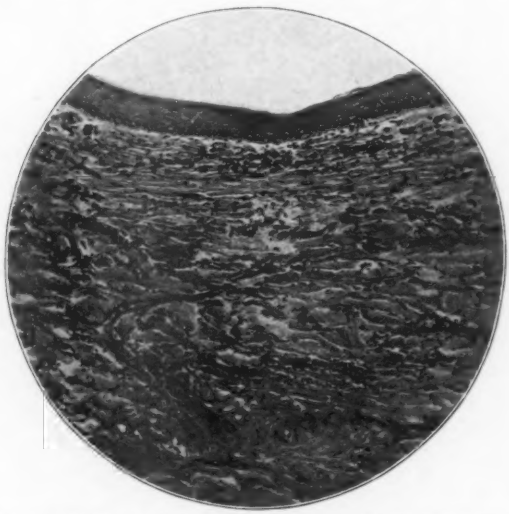

FIG. 6.—Showing similar changes as in Fig. 5, but with advanced atrophy of the epithelium.

The backs of the hands presented a smooth, translucent, atrophic skin, with numerous dark-brown lentigines and tortuous veins underneath, which, together with the tendons, shone through the integument.

Over the ulnar aspect of the right forearm a well-defined, partly erythematous and partly pale, atrophic band of skin was present, extending from the dorsal surface of the wrist to the elbow. With the exception of a small, atrophic patch half-way between the wrist and elbow this area was rose red in color, smooth, glistening, somewhat translucent, and showing a tendency to become bound down to the underlying tissues. There was no palpable infiltration. At the elbow, with the arm fully extended, the characteristic "cigarette-paper wrinkling" was present. Here the skin resembled

the appearances described as being present around the knee-joint: the integument was loose, pink, wrinkled, flaccid, and appeared to be redundant. The edges of this atrophic band merged gradually with the normal skin of the forearm, showing only an indefinite line of demarcation between healthy and diseased skin.

There was complete absence of hair follicles and glandular orifices in the diseased areas, lending to the skin the peculiar "naked" appearance characteristic of diffuse atrophies.

The appendages of the skin were normal, as were also the visible mucous membranes. Dentition was normal. There was no adenopathy.

The patient's urine was examined frequently, and under a moderately restricted diet it remained free from the abnormal constituents which it contained when she first entered the clinic.

HISTOPATHOLOGY. Sections for histological study were removed from the skin of the lower third of the flexor surface of the thigh, above the popliteal space. One large piece of skin, together with the subcutaneous tissue, was excised under 1 per cent. cocain solution. It consisted of a small nodule with its surrounding atrophic integument. The tissue was fixed in 10 per cent. formalin solution, dehydrated in alcohol and acetone, imbedded and cut in paraffin. The sections were stained with hematoxylin-eosin, polychrome-methylene blue, Weigert's elastic-tissue stain, Hansen's stain, and hematoxylin-orange G.

Two distinct varieties of pathological changes were readily demonstrable—namely, atrophy and fibrosis. One merged into the other, some areas showing advanced fibrosis, while in others the atrophy was the predominating feature. In the latter there were small areas of round-cell infiltrations, the remnants of the hypertrophic stage of the dermatosis.

In the stratum corneum there was a marked hyperkeratosis, manifesting itself by the laminated arrangement and the distinct separation of the horny layer. The stratum lucidum was poorly defined, being absent in many places. The stratum granulosum consisted of two or three layers of cells, a large number of which showed distinct vacuolization; many nuclei appeared intact, resisting the keratohyalin degeneration. The stratum spinulosum was attenuated, and here, also, many cells showed vacuolization. The intercellular spaces were much narrowed, the cell walls lying almost adjacent to each other. Marked degeneration was manifest, some of the nuclei failing to take the stain. The basal-cell layer, while intact in some places, had in many areas lost its columnar shape and regular arrangement, the protoplasm showing extensive cloudy swelling. There was a total loss of interpapillary pegs, the junction between epithelium and derma appearing almost as a straight line.

In the pars papillaris of the corium there was a total absence of

papillæ and marked degeneration of the collagen, the few remaining degenerated fibers showing a fine fibrillation, the fibers being widely separated and edematous. Scattered throughout this area were seen small mononuclear lymphocytes, together with many plasma cells. The bloodvessels showed distinct endothelial proliferation, the walls of the smaller ones being markedly thickened. The infiltration was not more pronounced in the vicinity of the bloodvessels than elsewhere. There was complete absence of elastic tissue in the upper portion of the pars papillaris; lower down a few fine fibers, showing multiple fractures, were still present.

In the pars reticularis the collagenous material was almost entirely replaced by edematous fibrous tissue, the small-cell infiltration being less pronounced than in the pars papillaris. This region showed areas of fibrous tissue arranged in a roughly stellate manner, around a tiny central fibrous nodule. Here and there were seen a few areas of circumscribed cellular infiltrations, consisting of lymphocytic and plasma cells, together with a few fibroblasts. Marked endothelial and perithelial proliferation was seen in some of the bloodvessels in these infiltrated areas as well as dilatation of the lymph spaces. The walls of the bloodvessels were thickened, some of their lumina being totally obliterated.

There was a total absence of hair follicles and sebaceous glands, while the remaining coil glands showed marked degeneration, the epithelium being absent in a large number of them. A considerable cellular infiltration was present around the coil glands, composed of plasma cells and lymphocytes. The arrectores muscles were few in number and showed extensive cloudy swelling and atrophy. The elastic tissue was markedly reduced throughout, the still remaining fibers being very fine, showing multiple fractures and cloudy swelling. The subcutaneous fat was present in normal amount.

This histological picture is almost the exact counterpart of many, if not most, of the microscopic appearances of the sections obtained from this type of atrophy, as recorded in the literature. It is practically identical with the findings recorded in our first patient, with this exception: In Case 1 we examined sections showing three stages of the disease — namely, hypertrophy, atrophy, fibrosis; in Case 2, the hypertrophic or infiltrative stage of the malady having run its course, we have left only the final atrophy and fibrosis. Evidences of the preëxisting hypertrophic stage were, however, manifested also in our second patient by the presence of the small areas of round-cell infiltrations as described above.

Clinical Considerations. If we compare the dermatoses presented by our two patients from a clinical point of view, we are at once impressed by the fact that the hypertrophic lesions, which comprised the most interesting feature of Case 1, were so few and scattered in our second case that they may have passed

by unnoticed had they not been sought for. Such a circumstance adds added emphasis to what has already been pointed out—namely, that the disease presents totally different types of lesions, depending upon its evolutionary states or cycles of development. In our second patient the transition from hypertrophy to atrophy and anetodermia was probably a much more rapid process than in the patient we described in our first report. The existence of the hypertrophic lesions in Case 2, small and inconspicuous though they may be, again supports the contentions of Herxheimer and Hartmann, who declare that the atrophic phenomena are, at some time or other in the course of the disease, preceded by infiltrative lesions. On section these infiltrations show characteristic cell aggregations of lymphocytes and plasma cells. They must not be confounded with the peculiar fibrous nodules, which occur in the final stages of some cases of acrodermatitis chronica atrophicans (Ketron[22]).

The occurrence of sclerodermia-like areas on the lower extremities of many cases of the disease is a subject which has aroused much interest among those who have studied this dermatosis. Numerous instances have been recorded (Finger and Oppenheim,[23] Herxheimer,[24] Arndt,[25] Heuck,[26] Kingsbury,[27] Kanoky and Sutton,[28] and many others). In nearly all long-standing cases of the disease we are confronted with two types of atrophy, which, clinically, are diametrically opposite in appearance. The skin of the knees, for example, presents the picture of a rose-red, flaccid, wrinkled and folded, translucent and velvety type of atrophy—the anetodermia of Jadassohn. The dorsum of the feet and the lower legs, on the contrary, are covered by an envelope of skin which is hard, tense and drawn, bound down, somewhat opaque, waxy or pale yellow, smooth and glistening—a sclerodermia-like form of atrophy. In the first type the redundant skin may be readily lifted between the fingers; in the second the tense skin cannot even be grasped between the fingers or lifted from the underlying tissues. As Finger has pointed out, the occurrence of these sclerodermia-like areas in acrodermatitis chronica atrophicans has been the cause of frequent errors in diagnosis, many of the cases having been relegated to the sclerodermia group of dermatoses (Jakobson,[29] for example).

"With regard to the relationship existing between anetodermia

[22] Dermatitis Atrophicans, with Report of a Case showing Fibroid Formations, Urol. and Cutan. Rev., 1913, i, p. 286.

[23] Loc. cit.

[24] Loc. cit.

[25] Verh. d. X Kong. deutsch. Dermat. Ges., 1908, p. 351.

[26] Acrodermatitis Chronica Atrophicans cum Sclerodermia, Ikon. Dermat., 1907, ii, plate x.

[27] Acrodermatitis Chronica Atrophicans with Sclerodermia, Jour. Cutan. Dis., September, 1907.

[28] Jour. Cutan. Dis., 1909, xxvii, 556.

[29] Berlin. dermat. Ges., 1906, v; Dermat. Zeitsch., 1906, xiii, p. 873.

and sclerodermia," says Finger,[30] "we have already called attention to the fact that a certain group of cases, the so-called morphea of French and English authors, give the impression of being transitional stages between the two diseases. It would be necessary to demonstrate a more intimate relationship between these two processes to convince me that anetodermia and sclerodermia may exist conjointly in the same individual. Their simultaneous occurrence would point to a common etiology. Such, however, is not the case. We have mentioned the fact that the diagnosis of sclerodermia has been made erroneously with reference to the infiltrated lesions of acrodermatitis chronica atrophicans as well as the tense forms of atrophy which occur in the course of diffuse anetodermia in those areas in thich the skin is naturally ("physiologically") more or less tense and drawn—namely, the dorsum of the foot and the lower leg, anteriorly. After a thorough perusal of the literature, I am unable to convince myself that a combination of the two forms of tissue changes may coexist; and if such a case does occur, it is an open question whether an etiological factor is common to both, or whether we are dealing merely with a coincidental appearance of two unrelated dermatoses . . . Taking into consideration the fact that all of the so-called atrophies begin with inflammatory phenomena, it would seem wiser not to employ the term "atrophies," but rather "atrophying dermatitides," to designate the two groups—namely, (1) anetodermias; dermatitides culminating in flaccid atrophy; (2) dermatitides culminating in tense atrophy."

Róna,[31] on the contrary, seemed to look upon the tense, bound-down, atrophic areas in acrodermatitis chronica atrophicans as being a true sclerodermia. In a discussion on the chronic atrophying dermatitides, he states: "To what extent sclerodermia and acrodermatitis atrophicans are inter-related, is a question which can be decided only after much further study, especially with relation to etiology. There seems to be little doubt, however, that the same pathogenic factor may give rise to the cutaneous changes resulting in typical sclerodermia, as well as typical acrodermatitis, for twelve cases have already (1908) been recorded in which the two diseases occurred simultaneously in the same individual."

Oppenheim[32] presented a patient with the sclerodermia-like areas on the lower legs, before the Xth Congress of the German Dermatological Society. He excised a piece of skin from the dorsum of the foot, in an area which presented the transition from the dense, yellowish to the soft, wrinkled and reddish integument;

[30] Die Hautatrophien (Atrophia diffusa, Anetodermie, Atrophia maculosa) und deren Verhaeltnis zur Sklerodermie, XVI Internat. Cong. Med., Budapest, 1910.

[31] Acrodermatitis Chronica Atrophicans, Verh. d. X Kong. Deutsch. dermat. Ges., 1908.

[32] Vehr. d. X Kong. Deutsch. dermat. Ges., 1908.

that is, a section in which two coexisting morbid processes were manifest to the naked eye.

The histological examination of the transitional portion of this section presented the following changes: absence of papillæ; attenuation of the epithelium over the atrophic area; almost normal epithelium over the thickened area. The connective tissue of the cutis was rather dense in the upper portions; the bloodvessels in the atrophic area were dilated, showed only moderate infiltration, their walls being but slightly altered; in the thickened portion there was much greater infiltration and no dilatation of the bloodvessels.

The chief changes affected the elastic tissue. In the atrophic portion this was totally absent in the upper layers of the cutis, but in other areas there were small islands of elastic fibers which showed structural changes; they were thickened, clumped, failed to take the elacin stain, but in the deeper layers of the cutis, they appeared to be normal. In the thickened portion the elastic fibers in the cutis were preserved up to the epithelial border; they were delicate, tortuous and wavy, and took the stain in a normal manner; there was a sharp line of demarcation between the areas in which the elastic fibers were present and in which they were absent.

"The significance of these histological findings point to the existence of a scar-like tissue, which may develop, as the result of secondary influences, from the atrophic tissue. We cannot regard these areas in the light of a sclerodermia on account of the absence of increase in collagen, absence of papillæ, and lack of bloodvessel changes; nor can we regard it as an atrophic stage, on account of the preservation of the elastica and because the clinical picture is strongly against such an assumption."

Evidently the question as to the true nature of the sclerodermia-like areas in acrodermatitis atrophicans will eventually be determined by further laboratory investigation. For it must be admitted that those observers who look upon them as being ordinary sclerodermia, base their opinion on clinical grounds alone.

The "ulnar band" and its analogue on the calf of the leg is so characteristic of the disease that it must be considered an important diagnostic factor in the differentiation of acrodermatitis atrophicans from other forms of diffuse cutaneous atrophies. Its absence, as has already been pointed out, is of little diagnostic significance, while its presence is a strongly corroborative symptom of the disease. Hertmanni[33] alone presented a series of seven consecutive cases from his clinic, in each of which the ulnar band was a prominent symptom.

As to the etiology of the disease, nothing is known definitely.

[33] Acrodermatitis Chronica Atrophicans, Verh. d. X Kong. Deutsch. dermat. Ges., 1908.

Oppenheim[34] thinks it may be partly due to intra-uterine pressure. A nervous origin, a tuberculous origin, and disturbances of internal secretions have all been considered by many authors. The existence of a transient glycosuria in our patient is probably an unrelated phenomenon, as the cutaneous changes began about ten years before any abnormal constituents in the urine were discovered. The patient gave a positive Wassermann test, but no other evidences of syphilis were discoverable. The coexistence of the disease with syphilis has been recorded on several occasions (Fordyce,[35] Grosz[36]). No definite conclusions can, of course, be drawn from such isolated instances.

The prognosis as to life is good. The disease is usually free of all subjective sensations, barring occasional itching, which is readily relieved by ordinary antipruritic applications. The majority of the patients seem to enjoy ordinary good health. The disease does not seem to shorten life, nor does it seem to make its victim more susceptible to intercurrent affections.

The treatment is purely palliative. In the early stages the application of dry heat, combined with injections of fibrolysin, are said to have given promising results. Patients suffering with pruritus and ulcerations on the legs, occurring as the result of malnutrition of the tissues, are treated by ordinary remedies, with good results. Arsenic and thyroid gland have been employed empirically.

Conclusion. We have, in acrodermatitis chronica atrophicans a distinct clinical variety of diffuse, progressive, atrophying dermatitis, possessing certain characteristic and more or less constant features, by means of which it may be differentiated from similar cutaneous pictures. These features are: (1) The presence of early inflammatory and infiltrating lesions, preceding or occurring together with atrophic changes; (2) the first evidences of the malady appearing usually on the hands and feet and progressing centripetally toward the trunk in an exceedingly slow and insidious manner; (3) the occurrence of the ulnar band or its analogue on the calf of the leg; (4) the relatively "immune area" below Poupart's ligament; (5) the anetodermia, most pronounced around the knees and elbows.

We extend our thanks to the staff of the dermatological clinic for its kindness in preparing sections, photographs, and photomicrographs of our case; and for the privelege of making use of the material from his clinic, we are greatly indebted to Prof. J. A. Fordyce.

[34] Etiology of Acrodermatitis Chronica Atrophicans, Wien. klin. Woch., 1912, xxv, p. 367.

[35] Symmetrical Cutaneous Atrophy with the Coincident Development of Syphilis, Jour. Cutan. Dis., 1904, xxii, p. 155.

[36] Atrophia maculosa auf dem Boden luetischer Effloreszensen, Wien. dermat. Ges., February, 1908.

THE SEQUENCE OF THE PATHOLOGICAL CHANGES IN ACUTE APPENDICITIS AND APPENDICULAR PERITONITIS.

By E. MacD. Stanton, M.D., F.A.C.S.,
SCHENECTADY, N. Y.

The study upon which this paper is based was originally undertaken with the idea of tracing the progress of the processes of inflammation and repair in cases of acute appendicitis both as regards the primary appendicular inflammation and the complicating peritonitis. During the course of the study I have examined microscopically 539 appendices removed during or within ten days following an acute attack, and I have studied the gross pathology as found at operation in more than fifteen hundred cases of appendicitis. In every instance the pathological data has been classified especially with reference to the duration of the symptoms previous to the time of the observation of the pathological conditions. As regards the appendicitis itself, the time was figured from the first onset of symptoms while as regards the more extensive peritoneal involvements it was found necessary to determine not only the time of the beginning of the attack but also approximately the time of occurrance of any exacerbations of peritoneal symptoms.

When the lesions are studied in this way in a sufficiently large series of cases the progress of the processes of inflammation and repair can be readily traced. Furthermore, it is apparent that most of the so-called varieties of acute appendicitis represent only different stages of development of the inflammatory process, and in spite of minor variations in the intensity and extent of the destructive process there is found to exist a striking general similarity in the fundamental pathological changes as they occur at each of the succeeding periods following the onset of symptoms.[1] In fact, if we stop viewing the appendices removed at operation as museum curiosities and study them as examples of a disease process, grouping them according to the day of the disease in which they are removed, it is surprising how fundamentally alike are the specimens removed during each succeeding day of the attack.

[1] We frequently hear statements to the effect that in appendicitis it is often impossible to predict with any degree of accuracy from the clinical symptoms the pathology existing in the abdomen. This is true as regards diagnoses based on the physical findings alone, but it should not be true as regards diagnoses based on the physical findings plus a good working knowledge of the pathology of each day of the disease. Given the date of the onset of attack, the time of any acute exacerbation of peritoneal symptoms, if such there has been, and the physicial findings as regards the extent of abdominal rigidity, and one should be able to predict the pathology with an accuracy not surpassed in any other intra-abdominal condition with which I am familiar.

Even more uniform is the sequence of changes in the complicating peritonitis, for if peritonitis be studied as a disease process it will be found that as regards any given area of involvement the lesions, of say eighteen hours' duration, present certain fundamental features which are essentially similar in each case. Likewise forty-eight hour cases present features typically characteristic of the forty-eight hour stage of the infection, and so on from day to day throughout the course of the disease.[2]

In this paper I shall not attempt to detail the occasional, and for practical purposes unimportant, variations from the usual progress of the disease. Those interested in this phase of the subject I would refer to Aschoff's monograph[3] on the pathology of appendicitis and to my paper published in 1905.[4]

It is interesting to note, however, that in the later cases studied by me the variations from the average have been much less noticeable than in the earlier cases, probably in part because of more accurate histories, but very largely because in most of the later cases the appendix and surrounding organs had been kept at rest by therapeutic means during the time between the onset of symptoms and the operation.

First Day. The pathological changes found during the first twenty-four hours of an attack of appendicitis are essentially similar in nearly all cases. I have never seen a real case of acute appendicitis operated at this stage of the disease in which a definite obstruction of the lumen of the appendix was not demonstrable. Proximal to this point of obstruction the appendices show little, if any, noteworthy pathological changes. Distal to the point of obstruction, the appendices are constantly distended to a point approximating the maximum distensibility of the organ. After the first eight or ten hours of the attack, fibrin is usually found on the peritoneal surface, and toward the close of the first twenty-four hours a considerable proportion of the appendices show macroscopic evidences of beginning gangrene. The true gross pathology of the first day of appendicitis can only be observed at the operating table because the loosening of peritoneal tissue bands incident to removal of the appendix, removes the causal obstruction or, if the obstruction is due to impacted fecolithes, these are often displaced

[2] This statement as regards the changes occurring in any given area of involved peritoneum is based not alone on the observations made in cases of appendicular peritonitis, but has been checked by observations made at operation and postmortem in peritonitis of widely different origins such as perforating gastric ulcer and ruptured pyosalpinx. The question as to the frequency with which these lesions under favorable conditions will progress to resolution or local abscess formation must be determined from actual experience. That it is the rule in cases of pelvic peritonitis is well known to all, but there is as yet a difference of opinion as to how frequently it actually does occur in unoperated cases of appendicular peritonitis.

[3] Die Wurmfortsatzentzundung, Jena, 1908.

[4] Stanton, E. MacD., The Sequence of Pathological Changes in Appendicitis, Jour. Amer. Med. Assoc., June 10, 1905.

during the manipulations so that by the time the appendix reaches the laboratory the complete picture of the gross pathology is usually lost.

The microscopic changes of the first day consist of an intense diffuse, polynuclear leukocytic infiltration with in all but the milder cases, focal areas of hemorrhages and necrosis involving all coats with a more or less extensive destruction of mucosa, and in many cases a fibrinous or fibrino-purulent exudate on the peritoneal surface. One of the most striking features in these early cases is the presence throughout the majority of the sections of numerous focal areas of necrosis. These areas are larger but are not as a rule more numerous in those cases which show macroscopic evidences of gangrene.

Many writers on the pathology of appendicitis would have us believe that acute appendicitis begins as a catarrhal inflammation of the mucosa, extending to the lymphoid tissue of the submucosa and finally through the muscular coats to the peritoneum, thus inferring that so-called catarrhal appendicitis is an early stage of the acute process. In ten years' time, in which I have made a microscopic examination of practically every first-day appendix that I could lay my hands on, I have never found a single instance of catarrhal appendicitis in a specimen removed during the acute stage of the attack. The diffuse infiltration of all coats is demonstrable even in cases operated within five or six hours of the onset of the first symptoms. Moreover, I have never seen an example of so-called catarrhal appendicitis diagnosed as such by other pathologists which, on referring back to the clinical history, did not prove to be either an appendix removed at an interval operation or a symptomless appendix removed incidental to other intra-abdominal surgery.[5] I believe this question of catarrhal appendicitis is worthy of emphasis for I am certain that the acceptance on the part of general practitioners and surgeons of the belief that catarrhal appendicitis is really a clinically important pathological entity has led to many grave errors in the field of appendiceal surgery.

The peritoneal lesion of this first day is essentially a fibrinous or serofibrinous exudate. On the surface of and in the immediate neighborhood of the appendix the primary exudate seems always to be of a dry, fibrinous character. In the cases studied by me extensive serous exudates have been found only toward the close of the first twenty-four hours of the attack, and then only in cases which had been given strong cathartics soon after the onset of the symptoms.

Even in the presence of a fluid exudate of greater or less extent

[5] Kocher (Cor. Bl. f. Schweize Aerzte Basel, 1913, xliii, 1633) in a recent discussion of this subject says, "I see appendicitis catarrhalis only as a chronic form and as a residue after earlier acute attacks."

at this stage of the disease the general peritoneum is smooth, and aside from a more or less intense congestion of the subendothelial bloodvessels there is little evidence of a true peritonitis.

From a surgical view-point I believe that the peritoneal involvement of the first day may in nearly all cases be ignored and the abdomen closed without drainage. This assertion is, I am certain, borne out by clinical experience, and bacteriological studies (Kelly,[6] Watzold,[7] Cohn,[8] Aschoff,[9] DeQuervain[10]) show that in the majority of cases this first-day exudate is free from bacteria.

I have dealt somewhat at length on the first day's pathology in acute appendicitis because it is the foundation upon which the subsequent course of the disease is based.[11]

SECOND DAY. Beginning with the second day of the attack, the peritoneal involvement, which is present to a greater or less extent in over half of the cases, assumes great practical importance and from now on we are really dealing in the majority of cases with two pathological conditions which must be described separately. First the inflammed appendix, and second the associated peritoneal infection.

In the appendix itself we find a continuation of the inflammatory process begun on the first day. Owing to a coalescence of the microscopic areas of necrosis seen in the first day cases there is by the second day a decided increase in the frequency of macroscopic areas of gangrene. Gross perforation of the appendix itself, with or without gangrene, if it is going to occur at all usually takes place before the end of the second day.[12]

Microscopically, second-day appendices show an intense leukocytic infiltration involving all coats together with a more or less extensive ulceration of the mucosa, while over 70 per cent. show

[6] The Vermiform Appendix, 1905.
[7] Quoted by Aschoff.
[8] Arch. f. klin. Chir., Bd. 85, Heft 3.
[9] Loc. cit.
[10] Cor.-Bl. f. Schweize Aerzte, 1913, xliii.

[11] I believe that the pathology of this first day corresponds closely with the clinical symptoms. First, we have the obstruction causing the primary colic which, like all other colics originating in the gastro-intestinal tract, is, as a rule, referred by the patient to the pit of the stomach or mid-abdominal region. As in gall-stones, strangulated hernia and other obstructive lesions in the gastro-intestinal tract this colic is usually accompanied by nausea and vomiting. It is interesting to note that pressure over the appendix at this very early stage often causes an increase in the pain referred to the umbilical region. A few hours later, with the development of the inflammatory reaction in the appendix, we have a new subjective pain due to the inflammation itself and referred by the patient to the region of the appendix. Local tenderness and rigidity apparently develop with the first involvement of the peritoneal covering of the appendix.

[12] The term perforation as applied clinically and meaning a sudden increase in peritoneal involvement has, I believe, little definite relationship to gross perforations of the appendix itself but rather to the sudden giving away of adhesions limiting a peri-appendicular infection. Histological studies would seem to show that the great majority of appendices are bacteriologically perforated early in the attack, and that protection of the general peritoneal cavity against the infection depends far more upon the maintainance of the integrity of the fibrinous protecting adhesions surrounding the appendix than upon the bacterial impermeability of the inflammed wall of the appendix itself.

a well-marked fibrinopurulent exudate on the peritoneal surface. In those cases which presented macroscopic evidences of gangrene the areas of necrosis as seen microscopically are decidedly more extensive than in the similar cases of the first day group, while in those cases which did not present microscopic evidences of gangrene the focal areas of necrosis, so prominent in the first day cases, are still evident in the majority of sections, but are often obscured by the leukocytic infiltration.

THIRD DAY. By the third day the destructive process in the appendix itself has, in the majority of cases, reached its maximum both as regards the macroscopic and microscopic evidences of disease.

Histologically, the third-day appendices show a diffuse inflammation of the same character as that seen in earlier groups. In the macroscopically gangrenous cases the necrosis is prominent, while in the non-gangrenous cases focal areas of necrosis are seen only in the mucosa. The most striking histological feature which distinguishes this group from the earlier groups is the evidence of beginning repair as seen by the presence of fibroblasts in all sections. These new-formed connective-tissue cells are especially numerous in the region of the peritoneum, although present in other areas, particularly in those cases showing the least marked leukocytic infiltration.

From the third day on changes in the appendix itself have chiefly to do with the process of repair which proceeds with surprising rapidity, the histological picture varying from day to day in the same manner as in any other inflammatory process undergoing repair by organization. However, the rapidity of the repair varies considerably in different cases, being slowest in those cases accompanied by extensive gangrene and most rapid in those cases accompanied by the least primary destruction.

FOURTH DAY. The fourth day is characterized chiefly by an increase in the evidences of repair. Microscopically the gangrenous cases show large areas of complete necrosis, the histologic picture differing but little from that seen in the gangrenous cases of the third-day group. In sections of the non-gangrenous cases and in sections taken at some distance from the necrotic areas in the gangrenous appendices, the most noticable histologic feature which distinguishes this group from the preceding one is a decided increase in the relative number of fibroblasts and the presence of numerous lymphocytes, and in many cases plasma cells. In those cases accompanied by a peri-appendicular exudate a few fibroblasts and many new-formed bloodvessels can be seen extending into the exudate from the peritoneal surface. Focal areas of hemorrhage into the exudate occurring from these new-formed bloodvessels and frequently seen in the sections.

FIFTH DAY. The microscopic lesions of the fifth day may be classified into two rather sharply defined groups. In the cases presenting macroscopic evidences of gangrene, the necrosis and polynuclear leukocytic infiltration is still the predominating characteristic, although the repair process is well advanced in some instances. In the non-gangrenous cases the polynuclear leukocytes have practically disappeared except at the surfaces of the ulcerations in the mucosa and of the peri-appendicular exudates. Throughout the coats of the appendix there is a marked increase in the number of fibroblasts and often an intense lymphocytic infiltration. In the peri-appendicular exudates the new-formed bloodvessels penetrate to a greater distance than in the fourth-day group, and this granulation tissue is decidedly richer in fibroblasts.

SIXTH AND SEVENTH DAYS. Histologically, the repair processes are seen on the sixth and seventh days are decidedly more advanced than in the fifth-day group. The gangrenous cases show well-marked evidences of repair, the histological picture of which is similar to that seen in the non-gangrenous cases of the preceding group. The non-gangrenous cases now show areas in which the fibroblasts are massed together and elongated so as to resemble young connective tissue cells. Small ulcers in the mucosa have apparently been largely repaired.

SECOND WEEK. After the first six or seven days the repair processes in all but the most extensively damaged organs are so far advanced as to present microscopic pictures of a subacute or chronic character. Even in the more severely damaged appendices the repair proceeds rapidly, and as a rule results ultimately in a surprisingly complete restitution of the organ.

Acute recurrences following dietary or other causes if they occur at this stage result in the engrafting of a new acute lesion upon the histological picture of partial repair. Evidences of this type of acute recurrence were rather common in my earlier cases, but while I suspect the too free use of cathartics and dietary errors as the cause I have not been able to collect any really trustworthy evidence on this point. The fact remains, however, that in more recent years I have not observed more than three or four appendices showing an acute lesion engrafted upon a subacute process.

APPENDICULAR PERITONITIS. Before describing the progress of the pathological changes associated with the complicating peritoneal infection I would emphasize the fact that the distribution of this infection in the peritoneal cavity seems to be dependent very largely upon purely mechanical factors.

It is a popular assumption that the extent and seriousness of the peritoneal infection bears a rather definite relation to the extent of the destructive lesion in the appendix itself, but fluid exudates frequently occur without gangrene or actual perforation, and cases are frequently observed with extensive gangrene which must have

existed for several days without the presence of peri-appendicular pus, showing that other factors, such as the resistance of the patient, peristalic movements, and the virulence of the infecting organisms must play an important part in determining the character of the lesion during the early stages of the inflammation. Instead of finding gangrenous and perforated appendices associated with an extensive and severe peri-appendicular peritonitis it is the rule to find very limited peritoneal involvement, in spite of the most estensive destructive lesions of the appendix itself, in all of those cases referred by physicians who have from the first directed their treatment toward the prevention of the mechanical spread of the infection.

Surgeons may honestly differ as to the advisability of immediate operation in certain stages of the disease, but there can be no question as to the advisability of treating every case of even suspected appendicitis by the so-called Ochsner treatment until the diagnosis is possible, and the services of the surgeon procured.

In this connection I cannot do better than quote from Mr. Moynihan,[13] of Leeds, who says: "It is now about seven years since I was first brought firmly to the conviction that in cases of appendicitis it is the administration of an aperient that is responsible for the acute castastrophe of gangrene and perforation which ends in an acute peritonitis. I do not remember one single case that I have operated upon since in which it was not perfectly clear that the same sequence of events—pain, aperient, perforation—had occurred, and I therefore do not hesitate to say that in almost every instance of acute peritonitis due to the perforation of an appendix it is the treatment directed to the relief of the condition that is the cause of the serious and so often fatal catastrophe. The taking of a purgative medicine is something more than an impressive antecedent —it is, in my judgment, a definite cause. The only possible exceptions occur in those rare cases where direct violence gives rise to a rupture of the appendix or the laceration of the adhesions which enwrap it. In cases of appendicitis, however acute their origin may be, perforation followed by an acute general peritonitis does not seem to occur if no aperient is given and if absolute starvation is adopted from the first. The acute spreading or general peritonitis which occurs in this disease is due to treatment; it is a 'therapeutic peritonitis.' I am quite prepared to learn that this emphatic statement is received with a shrug of doubt and the tolerant smile of disbelief, but if strict inquiry is made into the intimate details of the history of the cases I cannot think that my experience of this disease will prove to be singular. In appendicitis, *perforation spells purgation*."

[13] Acute Emergencies of Abdominal Disease, British Med. Jour., April 1, 1911.

Deaver[14] emphasizes this same point as follows: "Perhaps the most important question that concerns the internist and practitioner, as well as the surgeon, is the use of purgatives during the acute stage of the disease. It is not long since we all thought that a purge should be administered in the initial stages of the disease, but we have come to realize that the contents of the bowel play practically no part in the continuation of the disease, while the peristalsis induced by purgation has proved to be a most unfavorable factor, defeating the end and principle upon which our treatment is based—namely, anatomical and physiological rest. The purgative is more deadly than the scalpel. Of this I have long been convinced, but with a view to obtaining exact figures to support my contention, I have had the year's work analyzed with respect to this point. Among 259 adults there were 79 that had a history of being purged before admission. Of these 79 cases all save 2, at the time of operation, showed appendices that were either perforated, gangrenous, acutely ulcerated, or surrounded by an abscess. The remaining 2 only were simple catarrhal inflammation. Of the 7 deaths occurring in the series 5 were purged before admission. Of those drastically purged, 97.5 per cent. showed the severest kinds of appendicular disease. The exact figures are here given:

"Pathological lesion of appendix: perforation, 30; gangrene, 9; acute ulcerative and suppurative, 23; peri-appendicular abscess, 15; acute catarrhal, 2.

"Among 100 children the same rule holds. There were 56 that had been vigorously purged. Of these, 86 per cent. showed the more serious lesions, such as gangrene, perforation, abscess, etc. Twelve cases had diffuse peritonitis, all of which had been purged before admission. The table is as follows:

"Pathological lesion: perforation, 22; gangrene, 15; acute ulcerative, 6; peri-appendicular abscess, 4; acute catarrhal, 8; indefinite, 1.

"In this series there were 44 acute cases that were not purged, and in this group there was but one case of perforation, 8 cases of gangrene, and no peri-appendicular abscesses."

My own conception based on pathological and clinical studies is that the great majority of appendices are bacteriologically perforated after the first few hours of the attack irrespective of whether or not there is a gross perforation or gangrene evident to the naked eye, and that the protection of the general peritoneal cavity from infection depends upon the maintainance of the integrity of the fibrinous peri-appendicular protecting adhesions rather than upon the bacterial impermeability of the wall of the appendix itself.

As stated above the peritoneal lesion of the first day of the attack is essentially a fibrinous or serofibrinous exudate. On the surface of and in the immediate neighborhood of the appendix the primary

[14] A Year's Work in Appendicitis, Trans. Coll. of Phys. of Philadelphia, 1912, xxxiv, 227.

exudate seems always to be essentially of a dry, fibrinous character. In cases studied by me extensive serous or seropurulent exudates have been found only toward the close of the first twenty-four hours of the attack, and then only in cases which had been given strong cathartics soon after the onset symptoms.

The peritoneal lesions encountered after the first day of an attack of appendicitis may be divided into two sharply defined groups: (1) those cases in which the inflammed appendix is protected from the general peritoneal cavity by a zone of fibrinous exudate massing together continguous intraperitoneal structures, usually the omentum, the head of the cecum, a portion of the parietal peritoneum, and one or two loops of small intestines, with or without a localized collection of pus in the immediate vicinity of the appendix, and (2) cases with more or less diffuse peritoneal involvement. It is this latter class of cases which gives to appendicitis its mortality, and it is of the greatest practical importance for us to have a clear conception of the sequence of the pathological changes as they occur in this complication of appendicitis.

The time of onset of the more diffuse peritoneal involvement can nearly always be determined from the clinical history. Usually the onset of well marked peritoneal symptoms follows a few hours after the giving of a cathartic on the first or second day of the disease, although, we not infrequently find that the acute exacerbation of peritoneal symptoms occurs on the third or some subsequent day—a so-called late perforation. Such acute exacerbations are almost invariably the result of giving food or cathartics by mouth or of active muscular movements on the part of the patient. At operation these cases of late "perforation" show peritoneal lesions of different ages, almost invariably a lesion of limited extent in the region of the appendix with a pathological picture corresponding to the day of the disease and a more or less diffuse lesion with a pathology dating from the time of the acute exacerbation.

Cases operated during the first twenty-four hours following a so-called perforation show that the first exudate thrown out by the peritoneum under these conditions is essentially a fluid exudate, and at first of a distinctly serous or sero-purulent character.[15] The

[15] A. V. and E. Moschcowitz (Arch. f. klin. Chir., 1907, Bd. lxxxii, 707), in reporting the pathological findings in 313 cases of appendicitis accompanied by peritonitis, deny that they found any evidence that serous, seropurulent and purulent peritonitis represent different stages of the same process because figuring from onset of the attack of appendicitis there was only a slight difference in the time at which these three forms of peritonitis were encountered at operation. They believe that it is far more probable that the three forms represent differences in the virulence of the infection, and differences in reaction on the part of individual patients. Similar observations were made by me in my earlier studies when my data was limited to that found in hospital histories but this apparent contradiction to the usual phenomena of inflammation promptly disappeared when I began to study cases coming under my personal observation, and was able to determine not only the time of the onset of the primary appendicitis but approximately the time of onset of the complicating peritonitis.

peritoneal surfaces during the first few hours are still smooth, and aside from a moderate congestion of the subendothelial vessels, there is little change in the peritoneum itself. In fact, except for the extent of the distribution of the fluid exudate, it is usually difficult to say just how far the peritonitis really does extend.

Following the first outpouring of serum, which gives to the first day its predominating characteristic, we have a continued migration of leukocytes and production of fibrin so that by the second day the intraperitoneal exudate, which is usually of considerable extent, is found to be distinctly seropurulent or purulent in character. The peritoneal surfaces now show more or less loss of lustre with here and there adherent flakes of fibrin, but they do not as yet show the marked roughening seen after the beginning of organization on the third day, and the absence of well-defined limiting adhesions is still a noticeable feature of the pathology.

It is during this second day of the peritoneal involvement that the serous surfaces continue to lose their lustre and that the relatively harmless exudate of the first day changes to the distinctly purulent exudate so characteristic of the third day and later cases. Likewise it is at this period that the mortality in operative cases begins to rise very rapidly.

It is well to note here that Murphy[16] in his reports of so-called diffuse peritonitis deals entirely with peritoneal lesions of under forty-eight hours' duration. As far as I know, Murphy does not report a single case of over forty hours' duration, and in a discussion before the Chicago Medical Society he referred to the third and fourth day lesions as cases of "pocketed" peritonitis which corresponds to my own observations concerning the sequence of changes in peritonitis. In other words, we must remember that the "diffuse" lesion described by Murphy by the onward march of the pathological process ends about the close of the second day of a peritoneal infection.

By the third day the continued fibrin production, together with the leukocytic migration, has resulted in transforming our previously diffuse fluid exudate into irregularly pocketed collections of pus. Limiting adhesions are now fairly well developed in most instances, but the lesions are as yet of a decidedly diffuse character, the area involved being much more extensive than at a later period, and there is as yet little or no evidence of the formation of sharply defined abscess cavities. The gross changes in the involved peritoneum, especially in the immediate neighborhood of the appendix, are now very noticeable, due in part to the more abundant fibrin, but chiefly to the changes in the peritoneum incident to the beginning organization which seems in all cases first to become noticeable on the third day following the involvement of any given area of peritoneum.

[16] Perforative Peritonitis, Surg., Gyn., and Obst., June, 1908.

I believe that the subsequent course of the disease depends largely on whether or not the inflamed peritoneal surfaces are allowed to remain in the same relative position one to another. Certain it is if at this stage, or earlier, we put our peritoneum at rest by withholding food and cathartics and administering opiates in suitable quantities, we find that by the fourth or fifth day all fibrinous adhesions are being replaced by organizing granulation tissue which is also noticeable over the surfaces of the peritoneum in direct contact with the purulent fluid exudate. This granulation tissue serves not only to limit but to encapsulate the pus, and it is from this time on that the formation of definitely defined abscess cavities is observed. These abscesses are at first usually more or less multilocular but later become more localized to form, usually one well-defined cavity. The first evidences of the formation of a true abscess cavity are observed on the fifth or sixth day following the onset of the infection, although it is not until the seventh or eight day that the cavities become sharply defined with limiting adhesions firm enough to permit such manipulations as the packing away of the non-involved intestines without great danger of accidentally opening the abscess at some undesired point.

After the process of organization is well established on the fourth or fifth day there is every evidence of a progressive diminution in the extent of the peritoneal involvement which becomes less extensive as the abscess cavity becomes more sharply localized by the organizing adhesions.

This phase of the repair process which results in the more or less complete resolution of the peritoneal lesion beyond the immediate wall of the abscess has been well shown in a number of cases coming to operation on the tenth and eleventh days, the clinical picture in each having been on admission that of a severe diffuse peritonitis. In these cases the abscess cavities were surrounded by a narrow zone of organizing adhesions, while the peritoneum of the ascending colon and nearby loops of small intestines beyond the wall of the abscess cavity, although non-adherent, was thickened, reddish, and distinctly granular without fibrin or other evidences of an acute lesion. The clinical picture was on the third and fourth days undoubtedly that of a diffuse peritonitis, and this view is confirmed by the pathological findings as observed later at operation, although by the tenth or eleventh day the diffuse lesion had so far cleared up as to leave but slight, though unmistakable, evidences of its having existed.

Summary and Conclusions. In conclusion I would emphasize the following points:

1. Acute appendicitis is even during the first day of the attack a diffuse inflammatory process involving all coats of the appendix.

2. The destructive process in the appendix reaches its height on the second and third days of the disease. From the third day

on the subsequent changes occurring in the appendix itself have chiefly to do with the repair of the damage done during the earlier periods of the attack.

3. The diffuse inflammatory process involving the walls of the appendix is of such character that even without gross evidences of perforation the protection of the general peritoneal cavity from infection depends upon the maintainance of the integrity of the fibrinous periappendicular adhesions rather than upon the bacterial impermeability of the walls of the appendix itself.

4. My observations lead me to agree with Deaver, Moynihan, Ochsner and others when they state that clinical perforation would almost never occur if the general practitioner and the laity would appreciate the fact that in appendicitis "perforation spells purgation" and withhold cathartics during the early stages of suspected cases.

5. If in cases of diffuse peritonitis the peritoneal surfaces are put at rest by withholding food and cathartics by mouth the sequence of subsequent changes occurring in the involved area represents a definite and essentially uniform process tending to the resolution of the lesion or the formation of definitely circumscribed abscesses.

6. After the first thirty-six to forty-eight hours of a diffuse peritoneal infection the lesions encountered are of such a character as to be essentially undrainable and not well suited to surgical interference, a condition which continues until the period of localized abscess formation.

TUBERCULOSIS OF THE VULVA.

By Kenneth Bulkley, M.D.,
NEW YORK CITY.

Since Koch,[59] in 1882, published his paper, there has grown up an enormous literature on the subject of tuberculosis. Among this can be found in nearly every language excellent and complete descriptions of the disease in its various forms. But although the process in the more common locations has been frequently described, some of the rarer manifestations have received but meager attention. It is the object of this paper to report a new case of tuberculosis of the vulva and to collate the scattered literature on the subject.

The following case has recently come under my observation. Mrs. G. M., aged forty-one years, was first seen in October, 1913. Her history at that time was as follows: Married, husband suffering from pulmonary tuberculosis, but as far as could be ascertained

had no genital lesions. One normal delivery with healthy child twenty-two years previously. About seven years ago patient miscarried at five months. Five years ago she first noted a small raw area on the inner surface of the labia minora. This lesion has been progressive since that time. It has given no discomfort other than occasional moderate burning, but coitus has been painful. It has discharged moderately but persistently. There has been absolutely no history of hypertrophy. During the past five years a large number of non-operative attempts at healing have been made, without effect. Her genital history is otherwise negative. Menstruation regular, painless, and normal. In 1911 patient

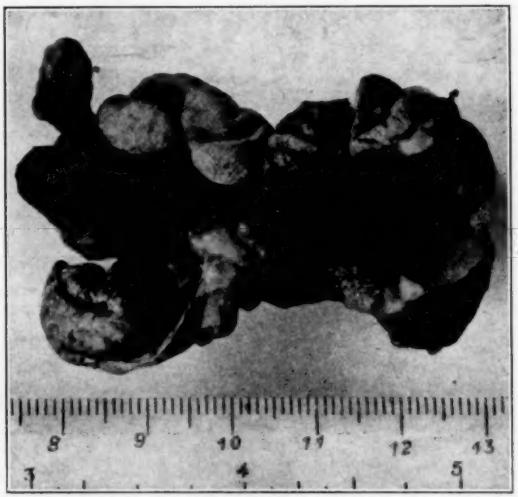

FIG. 1.—Excised specimen from author's case. Scale reads in centimeters and inches. View looking at ulcer surface. On the right the deep excavation anterior to the rectum; to the left the more shallow ulcer extending up the anterior vaginal wall. Between the two a narrower ulcer surface.

developed a pulmonary tuberculosis, for which she was treated in a sanitorium and finally discharged as cured. For the past year she has had no symptoms referable to the lungs.

Physical examination when first seen was as follows: A rather small-framed, wiry, thin woman, not anemic, and apparently in good general condition. Repeated examination of the chest failed to elicit any signs of active tuberculosis, nothing but relative dulness and some increased voice and fremitus remaining at both apices as evidence of her previous trouble. No enlargement of inguinal or other superficial lymph nodes. Abdomen and extremities apparently normal. Wassermann reaction negative.

Local examination disclosed the following: Uterus readily felt, retroflexed but freely movable without pain, fornices clear, no tenderness, no masses. Cervix shows old bilateral tear but is otherwise normal. Vaginal mucosa without lesion. Rectal examination negative, no stricture, fistula, or abscess. The left labia minora is replaced by an ulcer, the general shape of which is that of a dumb-bell, its long axis extending anteroposteriorly. It encroaches to a slight extent on the lateral vaginal wall above and on the inner surface of the labia majora below. Anteriorly its superficial diameter increases and reaches the vestibule and the edge of the urethra. Here it dips sharply upward along the anterior vaginal wall and parallel to the urethra to the depth of an inch.

FIG. 2.—Excised specimen from author's case. Scale reads in centimeters and inches. Lateral view showing the general dumb-bell shape of the lesion (somewhat distorted in fixation).

Posteriorly it shows a similar extension beneath the posterior vaginal and anterior rectal walls. There is no hypertrophy and no induration about the ulcer base or edge. The latter is a little irregular, well defined, rather poorly nourished, precipitous, and not undermined. The base of the ulcer is formed of irregularly disposed granulation tissue, grayish, edematous, not readily bleeding, not sensitive. Its surface is covered with a slimy mucus admixed with a moderate amount of pus.

In view of the tuberculous history, the duration of the lesion, the absence of anything suggestive of epithelioma, and the negative Wassermann reaction the case was considered as a tuberculous ulcer and excision advised. Under gas and ether anesthesia this was done on October 24, 1913. The entire labium majus, the region

of the labium minor, and a portion of the left lateral vaginal wall were excised *en masse*, together with the extensions along the urethra and rectum. Both these latter structures were preserved and the wound repaired by a modified perineorrhaphy. The immediate convalescence was smooth and, except for a small hematoma at the posterior portion of the wound, due to insufficient hemostasis at time of operation, the healing was by primary union.

A month later examination showed a small recurrence in the form of an ulcer at the urethral edge in the line of suture. As this lesion improved with the application of 10 per cent. silver nitrate, and as the patient gained twenty pounds in the two months following operation, it received no further treatment until February

FIG. 3 (× 175).—Author's case. Low-power photograph showing the slightly overhanging epithelium at the ulcer edge and the general character of the ulcer base.

24, 1914, four months after the initial operation. It was then thoroughly cauterized with the Paquelin cautery, and in two days the patient returned to her home out of the city.

Unfortunately the patient was not seen after this date. According to her own statements and those of her husband the area cauterized became smaller and was apparently in process of healing until the time of death. About two weeks after cauterization the patient began to run an irregularly intermittent and finally a continuous temperature. No definite physical signs to account for this temperature could be found by several physicians who examined her, but the prevailing opinion was that death, which occurred on April 8, 1914, was due to an acute general miliary tuberculosis. No autopsy was made. Locally healing continued until time of death.

Microscopic section shows an ulcer whose base is formed of granulation tissue everywhere infiltrated with small round cells and polymorphonuclear leukocytes. In the deep subcutaneous tissue beneath the ulcer base and also beneath the overlying epithelial edges surrounding the ulcer are found typical miliary tubercles. In the centres of the majority of these are collections of multinu-

FIG. 4 (× 100).—Author's case. Section taken a short distance from ulcer edge to show the great vascularity. To the left can be seen the deeper layers of the epithelium. Note the dilated and engorged bloodvessels and the beginning round-celled infiltration in the deeper layers of the section.

clear giant cells whose nuclei are arranged peripherally. About the ulcer margin some of these tubercles are found nearly reaching the deep layers of the epithelium. This latter is of normal thickness, and in some areas slightly cornified. There is a great increase in the number and size of the bloodvessels of the subcutaneous and submucous tissue about the ulcer edge. No tubercle bacilli can

be anywhere found. This is probably due to the fact that the specimen has been preserved for six months in alcohol.

HISTORICAL NOTE. Tuberculosis of the female genitalia was practically unknown until Morgagni,[75] in 1771, discovered at autopsy and described a case of tuberculosis of the tubes and uterus. This finding created at the time but little comment, for although there are scattered through the literature of the following years occasional references to the subject, no further contribution of note appears until a description by Raynaud,[84] in 1831, of a case of pulmonary tuberculosis in which there was an associated tuberculosis of the

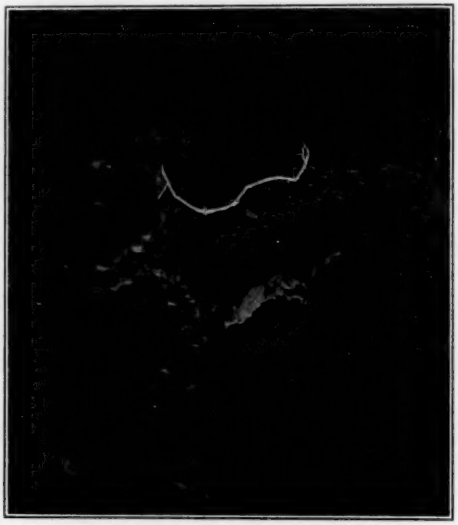

FIG. 5 (× 300).—Author's case. Section taken through the centre of a tubercle situated deeply in the connective tissue beneath the mucosa, to show the character of the giant cells.

uterus, tubes, and vagina. This is the first vaginal case reported. In 1849 Huguier[52] coined the unprecise term "esthiomene," and suggested that some of the cases might be due to tuberculosis. Interest in the subject increased rapidly from that date and numerous important and interesting observations were made. Bernutz,[7] in 1874, and Martineau,[71] in 1883, each reported cases of esthiomene, supposedly tuberculous. In the same year Babes[2] found tubercle bacilli in the vaginal secretion, and in the following year Mandach[67] reported the operative removal of tuberculous tubes and ovaries. It remained for Hegar,[50] in 1886, to thoroughly popu-

larize the subject clinically among the profession. Among the more recent articles in English dealing with the general subject of female genital tuberculosis should be mentioned the papers of Williams,[108] Senn,[93] and Murphy.[77]

Tuberculosis of the vulva as such has received far less attention. The first undoubted cases were reported independently, in 1881, by Cayla[13] and by Winckel,[109] although the cases of Bernutz,[7] in 1873, Cornil and Rigal,[18] in 1879, and others should, without question, be included in this class. Since 1881 many cases have been reported and not a few notable monographs placed on record. Among these should be especially mentioned articles by Bonnin,[9] in 1904, Bender,[4] in 1906, Combeléran,[17] in 1906, Daniel and Jianu,[21] in 1907, Stoica,[100] in 1907, Forgue and Massabuau,[36] in 1909, and Daniel,[20] in 1913.

Frequency. While statistics on the frequency of genital tuberculosis in women are readily obtainable, we have been unable to find any definite statistics relative to the frequency of involvement of the vulva in the tuberculous process. Its rarity is apparent not only from the fact that since 1881 only 71 cases have been reported, but also from the following statistics:

Geil[42] in 45 cases of tuberculosis of the uterus found no cases involving the vulva.

Mosler[76] in 47 cases of female genital tuberculosis found no cases involving the vulva.

Daurios[23] in 166 cases of female genital tuberculosis found no cases involving the vulva.

Beyea[8] collected 69 cases of cervical tuberculosis and found no cases involving the vulva.

Berkeley[6] among 8000 autopsies found genital tuberculosis 62 times and no cases involving the vulva.

Schiler[90] in 68 cases of genital tuberculosis found no cases involving the vulva.

Martin[70] in 53 cases of genital tuberculosis found no cases involving the vulva.

Simmonds[95] among 600 autopsies found genital tuberculosis 80 times and no cases involving the vulva.

Schlimpert[91] in 3514 autopsies found genital tuberculosis 73 times and no cases involving the vulva.

It is thus impossible to say in what percentage of cases of pulmonary, general miliary, or genital tuberculosis a localization in the vulva can be expected. Considering the fact that tuberculosis of the genitals is found in about 2 per cent. of cases coming to autopsy, showing other lesions of tuberculosis, and recalling the above figures, we must admit that the possibilty of vulva involvement is exceedingly small. That it occurs in animals as well as humans is shown by the report of Joest,[55] who describes a case of primary tuberculosis of the vulva in a cow.

Age. Bonnin[9] calls attention to the relative frequency of tuberculosis of the vulva in children. Table I (compiled from 72 cases) not only sustains this view, but shows that the disease is more common during the years of greatest sexual activity. A study of this table brings out the following points: Over 12 per cent. of the total number of cases occur during the first five years of life and nearly 17 per cent. before the tenth year. After that age there is a rapid fall in incidence, and no cases have been reported between the ages of ten and fifteen. As sexual life develops we see the possiblity of involvement increasing to such an extent that between the ages of twenty-five and forty one-third of the cases are found. With the subsidence of sexual activity comes a decline in incidence, so that after the age of fifty-five cases are but rarely seen. The youngest case in this series was seven months and the oldest eighty-eight years.

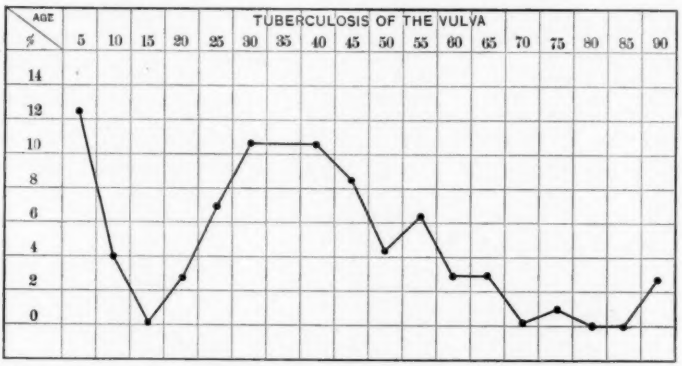

FIG. 6.—Table of age incidence compiled from sixty-two cases in the literature in which the age is given.

PATHOGENESIS. "As in all tuberculosis the bacillus of Koch is the condition *sine qua non* of the lesion." For infection to occur there must be not only local but also general causes. These latter do not concern us here, as they are of the same nature as those partially responsible for the development of tuberculosis elsewhere in the economy.

The local causes are, however, of importance, for in an individual predisposed to tuberculosis or already harboring a tuberculous focus elsewhere in the body these causes must operate for the localization of the infection at the vulva, whether it be primary or secondary. They may be grouped as inflammatory and traumatic.

Trauma is probably a factor tending to a certain extent to favor the localization of the infection. Experimentally, Popoff[80] was unable to produce genital tuberculosis in pigs or in rabbits

without traumatism. Gorowitz,[44] working independently, obtained similar results. In the 59 cases here reported above the age of fifteen years traumatism seems to have played some role. In 4 of these there was a definite history of injury either by a fall or by violent coitus; 23 cases are definitely stated to have had previous pregnancies, some of them going to full term, a number being instrumental, and a few terminating in abortion. In 32 cases the data is incomplete, but when we consider that these were all adults it is reasonable to suppose that some, at any rate, had borne children. It is worthy of notice that trauma is not mentioned in any of the 12 cases occurring before the age of ten years, but the source of infection can be reasonably traced in the majority of these children, and the trauma of handling and washing may have been sufficient not only for the *locus minoris resistensiæ*, but for the direct implantation of the bacilli. As Bonnin[9] says, "Traumatism, great or small, evident or unknown, appears after all as necessary for the development of tuberculous lesions in the region of the vulva."

Inflammation is also considered by some writers as playing a prominent role in the local predisposition to infection. Deschamps,[29] Jorfida,[56] and Combeléran[17] all lay emphasis on this, and point to acute simple vaginitis, gonorrheal vulvovaginitis, local manifestations of syphilis, simple ulceration, and excessive coitus as agents resulting in inflammatory processes predisposing to later tuberculous infection. In this connection it should be pointed out that a fair proportion of the cases in this series have been prostitutes.

Mode of Infection. The majority of authors in describing the mode of infection in vulvar tuberculosis have divided the cases into three groups, as follows: Primary vulvar tuberculosis, primary vulvar tuberculosis by auto-inoculation, and secondary vulvar tuberculosis. In the first group are placed those cases having no other focus of tuberculosis in the body. The second group comprises those cases in which the individual already harbors a tuberculous focus and infects herself by fingers, sputum, etc. The third group includes cases found in tuberculous subjects in which the vulva is infected by transmission of the bacillus within the body. This classification has seemed to us unnecessary. We will retain the first group as correct. The two following groups we will include under the heading of "secondary vulvar tuberculosis."

Primary Vulvar Tuberculosis. This is the most uncommon of the three forms, but that it does and can occur is indubitably proved by reported cases and experimental work. Popoff[80] and Gorowitz[44] have each been able to produce tuberculosis of the vulvovaginal mucosa in pigs and rabbits by the local deposit of tubercle bacilli after suitable traumatism. Among 47 cases of female genital tuberculosis Mosler[76] found 9 cases (19.5 per cent.) which he considered as primary. Among 119 cases Spaeth[97] considered 27

TABLE I.—CHRONOLOGICAL TABLE OF REPORTED CASES OF TUBERCULOSIS OF THE VULVA.

No	Year.	Reporter.	Age.	Type.	Parts involved.	Trauma.	Associated tuberculous lesions.	Treatment.	Results.	Remarks.
1	1881	Cayla[13]	42	Ulcer with hypertrophy	Entire introitus	1 child	Advanced pulmonary tuberculosis	None	Died	Anus and vulva a "cloaca" at time of death. Child died of tuberculosis.
2	1881	Winckel[109]	28	Ulcer with hypertrophy	Both labia minora	Miscarriage	None found	None	Died	Autopsy case.
3	1881	Winckel[109]	26	Ulcer with hypertrophy	One labia majora and minora	?	Tuberculous inguinal adenitis	None	Died	Autopsy case.
4	1884	MacDonald[66]	40	Ulcer	Entire vulva and perineum	Children	None found	None	Died after 2½ years	Lupus type.
5	1884	MacDonald[66]	33	Ulcer with hypertrophy	Right labia majora and minora	Injury by fall 2 years previous	None found	Curette and cautery	Well 1 year later	One child.
6	1884	MacDonald[66]	46	Ulcer with hypertrophy	Both labia majora	8 children	None found	Curette and cautery	"Cured;" end result ?	
7	1885	Deschamps[29]	25	Ulcer with hypertrophy	Labia minora and posterior commissure	Injury by fall 4 months previous	Advanced pulmonary tuberculosis and lupus of face and hand	Palliative	Died in 3 months	Prostitute. Autopsy showed other genitals normal.
8	?	DeFontaine[35]	40	Fistula	Labia majora	?	Tuberculous wrist and lungs	Cautery	Healed in 6 months	Fistula also communicating with rectum.
9	1886	Chiari[16]	30	Ulcer with hypertrophy	Clitoris, labia majora and minora	Injured during coitus 2 years previous	Tuberculous ulcers rectum. Autopsy showed general tuberculosis	None	Died	Autopsy case
10	1887	Demme[26]	13 mos.	Ulcer with hypertrophy	Labia minora	None	Tuberculous inguinal adenitis; tuberculous meningitis	Curette and cautery	Healed locally	Mother had pulmonary tuberculosis. Child died at 16 months of tuberculous meningitis.
11	1887	Demme[26]	7 mos.	Ulcer	Vulva	None	?	Curette and AgNO. No healing Healed after HNO	Well 2 years later	Father tuberculous.
12	1887	Demme[26]	15 mos.	Ulcer	Vulva	None	Tuberculous inguinal adenitis; pulmonary tuberculosis	None	Died	
13	1888	Zweigbaum[112]	32	Ulcer	Both labia minora and majora	?	Tuberculous lungs, vagina, and cervix; tuberculous rectovaginal fistula	Local	Died	Primary in cervix, then vagina infected, and then vulva.
14	1889	Weinlechner[107]	38	Ulcer	Entire side of introitus	3 children	None found	Cautery excision	Recurrence in 18 months; end result not given	Tuberculous ulcer developing on luetic base.
15	1890	Haeberlin[46]	27	Ulcer with hypertrophy	Both labia, majora, and minora and clitoris	1 child	None found	Excision	?	Father died of tuberculosis.

16	1891	Viatte[106]	32	Ulcer with hypertrophy	Left labia, majora, and minora	Married	None found	2 excisions; tuberculin	Cured	Recurrence after each incision; finally healed with Koch's tuberculin; lupus type.
17	1894	Emanuel[32]	?	Ulcer with hypertrophy	Posterior fourchette	No children	Tuberculous cervix and vagina	Hysterectomy	Died	Operative death following panhysterectomy. Autopsy showed generalized miliary tuberculosis. Vulva secondary to cervix.
18	1895	Martin[63]	23	Ulcer with hypertrophy	Left labia minora	?	Tuberculous lungs and rectum and rectovaginal fistula	None	Died	Vulva and rectum a veritable cloaca at time of death.
19	1895	Montgomery[74]	30	Ulcer with hypertrophy	Both labia majora	4 children	None found	None at time of report	?	Case demonstrated. Advised treatment with iodoform in collodion.
20	1896	Hintze[51]	?	Ulcer	Mons veneris, both labia and perineum	3 children	None found	Excision	?	Possibly a primary case.
21	1896	Kuttner[61]	6	Ulcer with hypertrophy	Right labia majora; mons veneris	?	Tuberculous lungs and inguinal glands	Excision	Well in 3 months	End result not given.
22	1896	Schenk[89]	4½	Ulcer	Both labia minora, clitoris and urethra	?	Tuberculous inguinal adenitis	Excision	Recovery; end result unknown	Possible primary case. Infection from tuberculous playmates by fingers.
23	1897	Karajan[57]	2	Ulcer with hypertrophy	Clitoris and labia majora	?	Secondary tuberculous ulcer of vagina	Excision	Recurrence	Possible primary case. No sign of tuberculosis elsewhere in body. Vaginal ulcer developed as recurrence after first operation.
24	1898	Havas[49]	21	Ulcer	Entire vaginal orifice	?	Pulmonary tuberculosis	?	?	
25	1896	Winter[110]	?	Ulcer	Labia minora	?	?	?	?	Pathologic specimen. Practically no data given.
26	1899	Brosin[13]	Old	Ulcer	Vulva	?	?	?	?	
27	1899	Davidsohn[24]	?	Ulcer	Vulva	Following severe labor	Generalized miliary tuberculosis	None	Died	Autopsy case; also tuberculous vagina.
28	1899	Fiocco and Levi[34]	52	Ulcer with hypertrophy	Vulva	?	?	Curette and cautery	Rapid healing	End result not given.
29	1899	Gebhard[41]	?	Ulcer with hypertrophy	Urethral edge	?	?	?	?	
30	1899	Gebhard[41]	?	Ulcer	Labia minora	?	?	?	?	
31	1899	Hansen[47]	4	Miliary tubercles	Vulva	?	Tuberculosis of kidneys, tubes, uterus, vagina.	None	Died	Autopsy case; supposedly primarily renal and involving other structures secondarily.
32	1899	Rieck[87]	39	Ulcer with hypertrophy	Labia minora	Married; children	None found	Excision	Cured	Husband had pulmonary tuberculosis; possible primary case.
33	1901	Ehrmann[30]	32	Ulcer	Urethral orifice	Prostitute	Pulmonary tuberculosis	Iodoform	Healed in 6 months	Prostitute.
34	1901	Ehrmann[30]	50	Ulcer	Labia majora and posterior commissure	?	?	Iodoform	?	Old case of syphilis.
35	1901	Ehrmann[30]	56	Ulcer with hypertrophy	Labia majora and posterior commissure	?	No sign of pulmonary tuberculosis	Excision		

TABLE I.—CHRONOLOGICAL TABLE OF REPORTED CASES OF TUBERCULOSIS OF THE VULVA—(Continued).

No	Year.	Reporter.	Age.	Type.	Parts involved.	Trauma.	Associated tuberculous lesions.	Treatment.	Results.	Remarks.
36	1901	Jorfida[56]	23	Ulcer with hypertrophy	Labia majora and posterior commissure	After delivery	Tuberculous vaginal ulcers; tuberculous inguinal adenitis	Excision	Cured	Supposedly infected by tuberculous friend.
37	1901	Martin[69]	32	Ulcer with hypertrophy	Labia majora	3 children	Pulmonary tuberculosis	Excised	"Primary cure"	End result not given; two sisters had tuberculosis.
38	1901	Rechenbach[55]	33	Ulcer with hypertrophy	Labia minora, clitoris, edge of urethra	4 children	No sign of tuberculosis elsewhere	Cautery and curette	?	
39	?	DePaoli[27]	?	Ulcer with hypertrophy	Both labia	?	?	?	?	
40	?	DePaoli[27]	?	Ulcer with hypertrophy	Both labia		Tuberculous intestine and peritonitis	?	?	
41	1902	Poeverlein[79]	49	Hypertrophy only	Labia majora	1 child	?	Excision	Recurrence in 4 weeks	End result not given. Diagnosis before operation "sarcoma."
42	1903	Petit and Bender[75]	33	Hypertrophy only	Both labia majora	Forceps delivery	No sign of tuberculosis elsewhere	Excision	Recurrence in 2 months	End result not given.
43	1904	Bender and Nandrot[5]	39	Ulcer with hypertrophy and fistula	Both labia majora	Local injury from fall	No sign of tuberculosis elsewhere	Excision and cautery	Remained cured	
44	1904	Chiarabba[15]	?	Ulcer with hypertrophy	Labia majora and minora	?	Tuberculous peritoneum, uterus, tubes, and cervix	?	?	
45	1904	Frattali[38]	19	Ulcer	Labia majora	?	Tuberculous inguinal adenitis; tuberculous ulcer vagina	?	?	Lupus type.
46	1904	Renaud[80]	4	Ulcer with hypertrophy	Left labia minora	None	No sign of tuberculosis elsewhere	Iodine and iodoform	Healed in 15 days	End result not given; supposedly a primary case of vulva infection.
47	1906	Audry and Combeléran[1]	1	Ulcer	Right labia minora	?	Tuberculous inguinal adenitis	Excision	?	Mother had pulmonary tuberculosis.
48	1906	Bender[4]	26	Hypertrophy only	Both labia minora	?	?	?	?	
49	1906	Combeléran[17]	50	Lupus	Right labia majora	?	None found	Excision	?	Lupus type.
50	1906	Dambrin and Clermont[19]	88	Abscess	Right vulva	?	Tuberculous osteitis of pubis	Incision	?	Secondary to tuberculosis of bone. Only case on record.
51	1906	Danlos, Pathaut and Gaston[22]	55	Ulcer with hypertrophy	Clitoris and labia minora	?	?	Excision	Recurrence in 6 months	End result not given.
52	1906	Hamburger[46]	3	Ulcer	Posterior commissure and labia minora	?	Tuberculous cervical and inguinal adenitis	Hygienic	Healed	Mother had pulmonary tuberculosis; sister died of tuberculous meningitis.
53	1906	Logothetopoulos[65]	75	Ulcer with hypertrophy	Urethral edge	No children	Pulmonary tuberculosis	Excision	Died	Operative death in 6 days.

54	1907	Daniel and Jianu[21]	45	Ulcer with hypertrophy	Both labia minora and clitoris	3 children	Tuberculous rectum	Excision	Healed	End result not given.
55	1907	Daniel and Jianu[21]	45	Ulcer with hypertrophy	Labia majora	?	No sign of tuberculosis elsewhere	Excision	Healed	End result not given.
56	1907	Meriel[73]	20	Hypertrophy only	Left labia minora	?	Pulmonary tuberculosis	Excision	Cured	Well locally 7 years later, but pulmonary condition slowly progressive.
57	1907	Meriel[73]	26	Ulcer	Labia minora	?	?	Excision	Healed	End result not given.
58	1907	Wolff[101]	51	Ulcer	Vulva	?	Pulmonary tuberculosis	Excision	?	End result not given.
59	1908	Boursier[10]	63	Hypertrophy only	Right labia majora	Children	Pulmonary tuberculosis	Excision	Healed	But. 2 years later, lesion of left labia minora.
60	1909	Forgue and Massabuau[36]	35	Hypertrophy only	Right labia majora	?	Tuberculous cervical and axillary adenitis; pulmonary tuberculosis	Excision	Recurrence	Recurrence in 10 months before death due to pulmonary tuberculosis.
61	1909	Kelly[58]	55	Ulcer	Anterior commissure	?	?	Excision	?	
62	1909	Lecène[54]	40	Bartholin's gland	Bartholin's gland	?	Possible tuberculous cervix	Excision	?	
63	1909	Lecène[54]	23	Ulcer and Bartholin's gland	Labia minora and Bartholin's gland	?	Pulmonary tuberculosis; tuberculous fistula in ano; tuberculous inguinal adenitis	Excision	Recovery	End result not given. Considered by author a blood infection.
64	1910	Kroemer[60]	44	Ulcer with hypertrophy	Vulva	5 children	?	Excision	?	
65	1910	Lagane[62]	6	Ulcer	Entire introitus	?	Pulmonary tuberculosis; tuberculous kidney and bladder	?	Died	Father had tuberculosis. Four brothers and sisters died of tuberculous meningitis. Case of probable secondary infection from kidney.
66	1910	Mauler[72]	37	Ulcers	Introitus		Tuberculous lungs, uterus, tubes, vagina, peritoneum, intestine, spine	None	Died	Autopsy case.
67	1910	Mauler[72]	41	Ulcers	Introitus	?	Tuberculous lungs, multiple joints, intestine, kidney, suprarenal, uterus, tubes, vagina, spine	None	Died	Autopsy case. Introitus involved by direct extension from vagina.
68	1910	Stoeckel[99]	28	Ulcer	Anterior commissure	Married	Miliary tuberculous intestine	Excision and cautery	Recovery	End result not given.
69	1911	Rossi[88]	87	Ulcer	Anterior commissure	?	Tuberculous lungs, uterus, cervix	None	Died	Autopsy case. Urinary passages normal.
70	1912	Brault[11]	7	Ulcer	Clitoris, labia majora and minora	?	No sign of tuberculosis elsewhere	Excision	Died	Early attempts at healing with chemical and thermal caustics without avail.
71	1913	Daniel[18]	36	Hypertrophy only	Right vulva and prepuce of clitoris	Miscarriages	Tuberculous inguinal adenitis	Excision	Recovery	End result not given. Husband had pulmonary and genital tuberculosis.
72	1914	Bulkley	41	Ulcer	Labia majora and minora	1 child; 1 miscarriage	Pulmonary tuberculosis	Excision	Recurrence; died	Died 6 months after operation with signs of an acute general miliary tuberculosis.

(24.5 per cent.) as primary. Numerous modes of infection have been suggested. Among them can be mentioned coitus, masturbation, clothing, pessaries, douche tips, wash-cloths, baths, toilets, the presence of tubercle bacilli in wash water, and air infection. Senn[93] considered most of the cases of all types infected by tuberculous sputum. Probably in the majority of cases, certainly of primary vulvar tuberculosis, infection occurs either by sputum or coitus. While it may be admitted that in any given case it is wellnigh impossible to point out with certainty the mode of infection, yet in a certain number of the cases in this series it seems fairly evident. We shall make no attempt to divide our cases into the two classes which we are now describing because of the manifest difficulty of doing so with any degree of accuracy. Nothing short of a complete postmortem on every case could make such a classification reasonably accurate. A few can be pointed out as examples of the probable mode of infection. In the two following cases the bacilli were probably derived from sputum. Schenk[89] describes a case involving the labia minora, clitoris, and urethra in a child four and one-half years old. This patient showed no other signs of tuberculosis, and repeated examinations of the chest were normal. It was later discovered that this child had a playmate with pulmonary tuberculosis, and the supposition is that the vulva was infected from tuberculous sputum probably transmitted by the fingers. Audry and Combeléran[1] describe a child of one year showing no other lesion of tuberculosis, who was probably infected from the soiled linen of the mother, who was tuberculous.

Much experimental and clinical evidence has accumulated in favor of the view that tuberculosis, local or generalized, can be transmitted from the male by coitus even in the absence of male genital tuberculosis. But here as before the local or general predisposition to infection plays its part, for when we consider the large number of cases of tuberculosis of the epididymis and prostate in married men, and the fact that very few of the wives of these men develop a tuberculous vulva, it at once becomes evident that coitus cannot always be incriminated. Some writers from this fact have argued that tuberculosis of the vulva is usually a descending infection, but Murphy suggests that the semen is usually transmitted beyond the vulva, into the vagina, and so the former escapes. Cohnheim,[14] in 1879, first suggested that genital tuberculosis might be transmitted by coitus. Corroborating this, Fernet[33] reported the cases of two women who after intercourse with tuberculous men developed local genital lesions. Glockner[43] has described a case of tuberculosis of the cervix due to coitus, and Verchère[104] has published similar cases. Straton[101] narrated an instance of a tuberculous growth in the vaginal wall of a previously healthy woman after marriage with a tuberculous husband. And finally Gaertner[40] inoculated the testes of rabbits and guinea-

pigs with tubercle bacilli and found that females fecundated by these developed tuberculosis and showed lesions of the vagina and uterus.

Verneuil[105] was the first to maintain that a tuberculous individual *without* genital lesions could transmit the bacillus by coitus, and the observations of others corroborate his view. Thus Spano[98] studied microscopically and by means of cultures the sperm of a patient dead of tuberculosis and found no bacilli. This same sperm, however, when inoculated into the peritoneal cavity of a guinea-pig gave positive results two out of three times. Sirene and Pernice[96] report amost identical experiments with the same outcome. Landouzy and Martin[63] using the sperm from a living patient obtained similar findings. Foa[35] succeeded in finding the bacillus in the sperm of men dead of tuberculosis but without genital lesions, while Jani[54] in 8 cases of phthisis found the bacilli five times in the testes and four times in the prostate, but was unable to find them in the sperm. And finally the work of Derville[28] is of interest. In 8 cases of genital tuberculosis in women he found the bacilli in the secretions of 5, and in examining the husbands and lovers of these women found that all had a tuberculous epididymitis.

Among the cases in the series here reported there are a number in which it is reasonable to suppose that the infection was by coitus. Thus in the case of Montgomery[74] there was no sign of tuberculosis elsewhere and no evident source of infection other than a husband probably tuberculous. In Rieck's[87] case also no other lesion could be found, and the husband was proved to be tuberculous. In our case also coitus may have been responsible, as the husband had an active pulmonary tuberculosis, but as far as could be ascertained no genital lesion.

Secondary Vulvar Tuberculosis. Secondary vulvar tuberculosis can occur from the transmission of the bacillus either without or within the body. It is then known respectively as primary vulvar tuberculosis by auto-inoculation (primary secondary tuberculosis [Pozzi[82]]) or as secondary vulvar tuberculosis. The first group includes all cases occurring in individuals having a focus of tuberculosis in the body from the discharge of which the tubercle bacilli are transmitted locally to the vulva outside of the body. Thus tuberculous sputum or tubercle bacilli from a discharging tuberculous bone sinus might be transmitted by means of fingers, clothing, wash-cloths, etc., to the vulva. Many authors consider that the majority of reported cases should be placed in this class.

The second group includes all cases in which there is a previous focus of tuberculosis in the individual and in which the path of infection lies within the body. In this type of lesion there are four possible routes of infection.

They are:

(*a*) Hematogenous.
(*b*) Lymphatic.
(*c*) Contiguity of tissue.
(*d*) Continuity of surface.

(*a*) *Hematogenous.* Although this path of infection is generally admitted there is very little conclusive evidence in the literature showing that it occurs with any regularity. Fiocco and Levi[34] believe that it is a common way for the distribution of bacilli, particularly in cases of tuberculous enteritis. Here they consider that the bacilli reach the mesenteric lymph nodes, then the thoracic duct, and in that way the blood current, and so are distributed to the vulva as well as elsewhere. The evidence is rather scanty, and in view of the more plausible and more nearly proved modes of infection the hematogenous route can safely be discarded except in theory. The only case in our series in which this path of infection seems fairly certain is that described by Hansen[47] in a child of four years, who at autopsy showed signs of a generalized miliary tuberculosis involving also the vulva, and even here the infection might have been from the urinary tract.

(*b*) *Lymphatic.* For anatomical reasons this mode of infection must be infrequent. The lymphatics of the vulva drain into the superior internal glands of the groin, and into these same glands drain the lymphatics from the lower central portion of the abdominal wall, the region of the anus and perineum, and the median surfaces of the buttocks. These channels all freely intercommunicate, and it is conceivable that a superficial tuberculous lesion of any of these regions might travel by way of the lymphatics and so reach the vulva. Practically this mode of infection is most difficult to differentiate from infection by contiguity of tissue. Thus in Martin's[69] case there was not only a tuberculosis of the vulva but a series of ulcerative lesions on the buttocks and upper inner thighs which was thought to be lupus. This is the only case in the series in which lymphatic infection seems even possible, but there are a number of cases in which ulcers of the lower rectum or anal canal might have infected the vulva by the lymphatic channels.*

(*c*) *Contiguity of Tissue.* It is possible to include more cases in this than in either of the two preceding classes, and in studying our material some unusual possibilities have presented themselves. Direct extension of tuberculous vaginal ulcers so as to include the vulva in the ulceration is the most common form encountered. After this we find direct extension from tuberculous lesions of the rectum. Here the vulvar lesion may present itself either as an

* The question has been raised as to whether a tuberculous infection can travel by the lymphatic channels against the normal direction of lymphatic flow. In this connection a case of tuberculosis of the breast reported by Power[81] is of interest. This was in a girl, aged fifteen years, in whom there was extensive axillary involvement and relatively little breast involvement. Powers believes that the axillary glands were the seat of infection and that the breast involvement was secondary.

ulcer or as a fistula. It is safe to say that direct extension by contiguity of tissue is most frequently from one of these two sources. Occasionally it may take place from tuberculous lesions of the skin, as already mentioned in the case described by Martin.[69] A most unusual case, and the only one of the sort we have been able to find in literature, has been described by Dambrin and Clermont[19] in a patient eighty-eight years of age. This patient, otherwise in good health, complained of a tumor of the right vulva. It was incised and found to be a cold abscess, originating in a tubercuous osteitis of the os pubis. Lecène[64] has published reports of two cases of tuberculosis of the vulva, both by direct extension of tuberculosis of Bartholin's glands. This is a unique observation, and is only paralleled in medical literature by the report of a case of tuberculous infection of Cowper's gland, the male analogue (Hartman and Lecène[48]).

(*d*) *Continuity of Surface.* The infection taking place under this head is believed to be derived from tubercle bacilli in the discharge either from the urinary system, genital system above the vulva, or from the feces from cases of tuberculous enteritis, etc. Examples of all of these three types of infection can be found in this series, and it might at first be thought that the constant passage of tubercle bacilli from one of these sources would lead to a frequent vulvar involvement. The fact is, however, that this does not occur with any great frequency, as can be readily judged from the figures already quoted as to the frequency of tuberculosis of the internal genitals and also from the frequency with which tuberculosis of the kidney and bladder is seen. In the 72 cases of vulvar tuberculosis here analyzed, lesions of the internal genitals are mentioned in only 9 patients who showed tuberculosis of the uterus five times, cervix five times, tubes four times, and vagina eight times. In only 3 cases is a tuberculosis of the kidney described, and only once tuberculosis of the bladder. The intestine has been involved but four times and the rectum but five times. We believe that too much stress has been laid by previous authors on this mode of infection.

Symptoms and Clinical Forms. Tuberculosis of the vulva clinically presents itself in a number of forms, some of which are more or less characteristic of the disease itself, while others are of such a nature as to rather mask the diagnosis. It has been the custom in the past to recognize three main forms of the disease. They are as follows:

(*a*) Hypertrophy with ulceration (*forme ulcereuse, forme ulcerogommeuse, chancre tuberculeuz*).

(*b*) Lupus type (*forme lupique*).

(*c*) Hypertrophy without ulceration.

In studying our collected cases it has seemed to us that this classification is either not comprehensive or is too sweeping. There

are undoubted cases reported which cannot be reasonably included under any of the above headings. Some of the cases which this paper considers are but scantily described, and we shall make no attempt to place each case in its class. We would, however, venture to suggest the following classification, into the divisions of which can be readily placed any given case in which sufficient data is reported.

1. Hypertrophy with ulceration.
2. Hypertrophy without ulceration.
3. Ulceration without hypertrophy.
4. Lupus type.
5. Fistulas and abscesses.

We will presently take up in detail the local findings in each of these five types, but before doing so it will be well to consider briefly the signs and symptoms common to them all.

The general symptoms are relatively slight and in primary vulvar tuberculosis comparatively negligible. In other cases they are in direct proportion to the amount of involvement of other organs. Here we see the general symptoms which may accompany tuberculosis of any part of the body, fever, increased pulse rate, loss of weight, anemia, etc.

Locally the subjective symptoms are often very slight until the disease is fairly well advanced. Burning or smarting, pruritus, or a vulvar enlargement may be the first symptom noted. With ulceration, especially if extending into the vagina, leucorrhea may be the first symptom, or possibly a burning urination, due to the passage of urine over a raw surface. Pain is usually not marked, except possibly during coitus. Functional symptoms are lacking in the absence of involvement of the internal genitals or urinary system. We cannot agree with the statement that hypertrophy is invariably present. Our case, as well as many in the literature, totally lacked this feature. The local findings in the various forms can be best described according to types.

1. *Hypertrophy with Ulceration.* This is the most common of all forms, and into this class the majority of cases can be placed. It is a disputed point as to whether the hypertrophy precedes the ulceration, or *vice versa*, or whether they develop hand in hand, but when first seen both processes are usually already evident. The hypertrophy may include the labia majora, minora, or the prepuce of the clitoris, or any of these parts may be involved singly or in combination with others. One side or both may be hypertrophied. The increase in size varies from small areas of leukoplakia of the mucous surface of the labia minora to tumor masses larger than two fists involving all the parts. This apparent hypertrophy may be an edema or a definite hyperplasia. Possibly it starts as the former, and continuing over a period of time gradually becomes transformed into the latter. When due to an edema the

surface appears smooth, tense, and uniform. There may or may not be discoloration. The margins are ill-defined and fade gradually into surrounding healthy tissue. The consistency is soft and depressions can readily be made with pressure of the examining finger. When due to hyperplasia the surface is of a rougher appearance, in color a little darker red, more nodular, its borders more precisely defined. The consistency is firm, brawny, and pitting is slight or absent. It corresponds more to the "elephantiatische tuberculose" of the Germans. There is seldom, if ever, any tenderness. It is questionable whether there are ever seen in this type the minute "apple-jelly" tubercles of true lupus.

Associated with this hypertrophy is ulceration, which varies in extent from minute areas the size of a pin-head to losses of tissue so great that the entire vulva, perineum, and anal region may be transformed into a veritable cloaca. These ulcerations occur with great frequency on the inner surface of the labia majora and minora, but may be found elsewhere. A quite frequent site is near the urethral edge or near the clitoris. At times they are a continuation of a vaginal ulceration. As already stated they frequently result in much loss of structure, so that it is not unusual to find an entire labia minora replaced by one of these ulcers. They may be single or multiple. Probably the larger single lesions represent the fusion of previous multiple ulcerations. Their irregular, indented borders are well defined, poorly nourished, seldom excavated, usually precipitous. Commonly superficial and not of greater depth than a quarter inch, these ulcers at times extend far into the subcutaneous or submucous surfaces. We have seen them extend in this manner to the depth of an inch. The base of the ulcer is formed of unhealthy granulation tissue, which shows its poor quality not only by its grayish, edematous appearance but also by the difficulty with which it can be induced to bleed. The surfaces of the lesions are covered with a rather profuse grayish, seropurulent discharge. They are seldom tender to the touch. The inguinal lymph nodes are often enlarged, at times due to definite tuberculous infection and at times due to a suppurative adenitis from absorption of the common pyogenic bacteria from the raw surface. Induration about or beneath the ulcer is usually absent.

2. *Hypertrophy without Ulceration.* This is an exceedingly rare form of which only 7 cases have been reported. Locally the findings are much the same as those already described in the previous section, lacking, of course the ulceration. The hypertrophy in these cases is usually due to hyperplasia and not to edema. Of the 7 reported cases 2 had an associated pulmonary tuberculosis and 3 a tuberculous inguinal adenitis. All occurred in adults.

3. *Ulceration without Hypertrophy.* In this group are placed all cases in which hypertrophy is not evident either from the history or examination of the patient. Many writers believe that such a

grouping is impossible because hypertrophy is always present, but our study of the collected cases has not convinced us on this point, and we believe that in a certain proportion of the patients, especially children, this hypertrophy is not found during any stage of the disease. In seven of twelve children under the age of ten years it was absent. The local examination of cases coming under this grouping shows ulcers similar in all respects to those already described, and needs no further comment. It is possible that some of the cases should be placed under the lupus type as late ulcerating lesions.

4. *Lupus Type.* That the vulva is a rare location for the development of lupus vulgaris so commonly seen about the face is shown by the statistics of Bender,[3] who among 380 cases of lupus found the vulva involved only once. The appearance, however, about the vulva differs but little from that of lupus elsewhere, except possibly for the fact of rather more frequent and early ulceration, due no doubt to the location upon a mucous membrane and the constant presence of moisture. There are the same brownish, rather deeply situated tubercles, fading on pressure to a yellowish color, giving the "apple-jelly" appearance, and being either single or multiple, with the tendency to grouping and confluence of multiple lesions to form a single lesion which early ulcerates. In some cases, as in one reported by Combeléran, the lesion may present itself as an apparent simple leucoplakia. Practically all of these lesions develop on the inner surface of the labia. It may be the development of these lesions, undetected until well advanced which contributes the majority of cases to the group we have called "ulceration without hypertrophy." Probably in this class should also be placed the occasional case in which there is a generalized miliary tuberculosis, including the vulva.

5. *Fistulas and Abscesses.* At certain times tuberculous lesions develop in the neighborhood of the vulva, caseate or become secondarily infected, and in seeking an exit for their contents, either distend one labia into a pus socket or perforate it, leaving through it a sinus which in course of time becomes lined with tuberculous granulation tissue. It is needless to point out that these must all of necessity be secondary tuberculous vulvar lesions. Thus a tuberculous osteitis of the os pubis has pointed at the vulva, a tuberculosis of Bartholin's gland has infected it, and tuberculous rectovulvar fistulas have been described. In all these cases, no matter what the point of origin, there will be present either an abscess or a fistula. The former can be identified as tuberculous only by a recognition of the primary focus, the latter in the same way or by the nature of the granulations lining the sinus, or by the recovery of tubercle bacilli in the discharge from it.

Pathology. While it is unnecessary to describe further the gross appearance of tuberculous lesions of the vulva as they occur

locally, it will be of interest to refer to the relative frequency of involvement of different portions of the vulva and to note the associated tuberculous lesions which in this series have been found in other parts of the body.

From the following brief tabulation it will be seen that the labia majora and minora are most frequently involved:

	Cases.
"Vulva"	10
Labia majora	29
Labia minora	30
Clitoris	8
Entire introitus	7
Posterior commissure	6
Anterior commissure	3
Mons Veneris	2
Edge of urethra	5
Bartholin's gland	2
Prepuce	1

The condition is more frequently unilateral than bilateral, and involvement of the labia majora and minora is the most frequent association.

Looking over our cases with a view to ascertaining what other portions of the body can be expected to show most frequently an associated tuberculosis, we obtain the statistics tabulated below. These must be judged only relatively, for their accuracy is marred not only by lack of complete reports but also by the fact that in the majority of cases the observations were clinical only, and not confirmed by autopsy record. The parts involved were as follows:

	Cases.
No associated tuberculosis mentioned or found in	31
Tuberculosis of lungs	21
" inguinal lymph nodes	11
" cervical lymph nodes	2
" axillary lymph nodes	1
General miliary tuberculosis	4
Tuberculosis of joints	2
" spine	2
" os pubis	1
" kidneys	3
" bladder	1
" suprarenal glands	1
" uterus, body	5
" uterus, cervix	5
" tubes	4
" vagina	8
" peritoneum	3
" intestine	4
" rectum	5
" meninges	1
" skin (lupus vulgaris)	1

It is thus seen that an associated pulmonary lesion is most frequently found and next in order a tuberculous lesion of some higher portion of the genital tract.

In describing the microscopic picture we can conveniently divide the lesions into two types, deep and superficial. To the former belong the four following clinical groups: hypertrophy with ulceration, hypertrophy without ulceration, ulceration without hypertrophy, fistulas and abscesses. To the latter belongs the lupus group. In the former the lesions are deep and involve not only the epidermis and derma or the mucosa and tissue immediately beneath it, as the case may be, but also the subcutaneous or submucous tissue. In the latter the superficial structures only are involved.

In the deep form the variation from the normal is as follows: The epithelium is at times perfectly normal and without noticeable alteration except, of course, where there is loss of surface. At times it is thickened and cornified. There is sometimes, but not always, seen in the derma an infiltration of plasma cells clustered together in masses in the centres of which may or may not be found giant cells. The lesions are especially marked and at times only seen in the subcutaneous or submucous tissue. This infiltration may be diffuse and lacking in giant-cell formation, due, as Unna[102] has shown, to lack of pressure and the elasticity of the parts involved. The white and elastic fibers are increased in size and swollen with a clear fluid. They present the appearance of a chronic edema. Many dilated bloodvessels and lymphatic spaces are seen. In the centres of and about the giant cells and diffusely scattered in the areas of diffuse plasma-cell infiltration tubercle bacilli can be found.

As they progress these lesions reach the surface and ulceration ensues. This process may take place only in parts of the lesion, usually the centre. The extent of the diseased area cannot therefore be judged alone by the extent of the ulceration. In some cases, as in the one described by Bender and Nandrot,[5] we find lesions on the point of involving the epidermis or mucous membrane, but the latter still preserved. Such findings substantiate the view held by some writers that the hypertrophic form of tuberculosis of the vulva represents delayed ulceration and is in reality the preulcerative stage of hypertrophy with ulceration. This delay in ulceration may possibly be due to the thickening and cornification of the epidermis which is more marked in the pure hypertrophic form than in the type with ulceration, where it is practically wholly lacking.

In the superficial form (lupus type) the lesions are confined to the surface layers and do not differ from the well-known picture of lupus as seen on the more common locations. They need not here be described other than to again emphasize the fact that the subcutaneous tissue is not involved.

Differential Diagnosis. The lesions which simulate tuberculosis of the vulva may be either acute or chronic.

Among the acute non-tuberculous lesions which may show ulcerations are gonorrheal vulvovaginitis, anogenital diphtheria, the ulcerations occasionally seen in the acute exanthemata, gangrene of the vulva in the eruptive fevers, acute Bartholinitis, and acute phagedenic and round ulcers (Vautrin[103]). In all of these the acuteness of onset, the presence of other local or general phenomena, and the bacteriological examination of the secretions are of essential diagnostic importance and need only be mentioned.

Greater difficulty in diagnosis will be encountered among the subacute and chronic lesions, as is shown by the use of the word "esthiomene." This term has been used to describe a chronic vulvar ulceration with or without hypertrophy, in the production of which a chronic lymph stasis plays an important role. Various lesions which should have received more accurate diagnoses have been described under this term. We agree with Bonnin,[9] who condemns the use of the word, and with Combeléran,[17] who points out that many cases described as "esthiomene" are true cases of tuberculosis of the vulva. Biopsy only will prove this point.

Syphilis of the vulva is encountered in a number of forms. The initial chancre is of more acute onset, the surrounding edema is of greater extent, the induration of the base more marked, the ulceration not so deep, the borders less excavated, and the granulations of a brighter red, than seen in tuberculosis. There is greater enlargement of the inguinal lymph glands than in tuberculosis. Microscopic examination of smears from the ulcer base will show the Treponema pallidum. In the mixed chancre the inflammatiory character of the lesion will be even more marked, and the bacillus of Ducrey will also be found. Syphilitic mucous patches of the inner surfaces of the labia can be differentiated from a tuberculous leucoplakia only by a search for the Treponema pallidum. *Late secondary* and *tertiary* syphilitic lesions of the vulva usually ulcerate and closely simulate tuberculosis. The ulcerations are, however, more acutely inflammatory and their granulations brighter. Microscopic examination of smears serve to differentiate them. Papulohypertrophic lesions of syphilis occasionally are confused with the hypertrophic form of tuberculosis. But in syphilis, fissures are usually present and the papillomatous character of the lesion is more marked. In all the various manifestations of syphilis about the vulva (except the early chancre) the presence of a positive Wassermann reaction establishes the diagnosis. Other evidences of the disease may be present. Rapid healing under specific treatment proves the luetic nature.

Simple chancre (chancroid) is frequently seen about the vulva. Here the acute onset, the greater pain and inflammation, the tendency for development of new lesions on coapted surfaces, the frequency of suppurative inguinal adenitis, and the microscopic finding of the bacillus of Ducrey should differentiate it from tuberculosis.

In *epithelioma of the vulva* the raised edges and hard nodular borders should identify the character of the lesion. They are not seen in tuberculosis. (Biopsy is conclusive.)

Sarcoma of the vulva is an exceedingly rare lesion, hard, firm, not ulcerating until a late stage, when metastatic lesions are already evident. In its early stages it is distinguished from the hypertrophic form of tuberculosis by its local character, involving one portion only of the vulva.

In *kraurosis vulvæ* the lesions are generalized and the skin and mucous membranes are grayish. Atrophy takes place to so great an extent that the labia majora and minora are much distorted and may be fused. This atrophy is not seen in tuberculosis.

Various *miscellaneous lesions* which may simulate tuberculosis have been mentioned in literature. None of them are of great importance and few of them should give rise to difficulty in diagnosis. Bonnin[9] refers to actinomycosis and molluscum contagiosum, both of which can be recognized microscopically. Combelèran[17] speaks of acne, furuncles, suppurative vulvar folliculitis, and herpes of the vulva. Froelich[39] has described a diabetic vulvar ulcer.

It is thus seen that there are many conditions from which tuberculosis of the vulva must be differentiated. In most of them a clinical diagnosis is possible, but the ultimate diagnosis must rest upon microscopic examination either of smears or of biopsy specimens.

Prognosis. We have reviewed the cases here collected to study the results of treatments used and to determine the prognosis. This latter is not good. In 23 cases the data as to immediate or late result is too meager for use in our study. In 49 cases such data is partially or wholly given. Of these 49 cases, 21 or nearly 43 per cent. died, while 28, or about 47 per cent., recovered. One case was reported well locally seven years after treatment, but when last seen had a steadily progressive pulmonary tuberculosis. Of the other cases reported "recovered" many were lost sight of shortly after treatment and some few have had recurrences. The true end-result was given in so few cases that the prognosis is probably even worse than the above figures indicate. An associated tuberculosis was found elsewhere in the body in all cases which died. There were two operative deaths recorded. One occurred from shock following a panhysterectomy for an associated tuberculosis of the body and cervix of the uterus; the cause of death in the second case was not given. Prognosis is no more favorable in one type of the disease than in another. The lupic type is considered by some writers more benign.

Table II shows briefly the results in this series of various forms of treatment. "Healed" and "recurrence" refer to the local condition for various intervals of time during which each case has been under observation. "Healed" cannot therefore be inter-

preted as an end-result, although for any individual case it may be such.

TABLE II.

	No. of cases.	Healed.	Recurrence.	Per cent. healed.
Excision	20	13	7	65
Curette and cautery	6	5	1	83
Excision with cautery	1	0	1	0
Cautery	1	1	0	100
Nitric acid	1	1	0	100
Iodoform	2	2	0	100
Tuberculin	1	1	0	100
General hygiene	1	1	0	100

TREATMENT. While the form of local treatment must vary with the individual case, the necessity of careful general management of the patient, rather than the disease, must not be lost sight of. It is unnecessary for us to here enter upon a discussion of the general treatment of tuberculosis. To suitable changes in diet, environment, and mode of life can be added, we believe with advantage, tuberculin. The details of technique, selection of patient and preparation, and dosage must be governed by those same rules which have given such excellent results in surgical tuberculosis elsewhere in the body. General miliary or active pulmonary tuberculosis contra-indicate the use of tuberculin.

The local treatment may be palliative or radical. Reference to Table II shows the results in this series of the different forms of treatment. Palliative measures vary in severity from the use of simple dusting powders or ointments to cauterization by mineral acids or heat. The value of local antiseptics is questionable and empirical. Iodoform, which is most frequently used, can be taken as an example. Fränkel[37] has shown that bacteriologically it is not antiseptic, and that after sterilization at high temperatures the iodin is driven off. Its chief value seems to be in its fibroplastic power. Because of this it may be useful in the treatment of localized tuberculosis. Fränkel,[37] however, prefers pure sterile bone carbon for this purpose. The pathology of the disease proves the uselessness of local applications which do not destroy. They cannot penetrate to the necessary depth.

The various caustics are also insufficient because of their lack of depth of action. Silver nitrate is worthless. The action of lactic and the mineral acids cannot be controlled. Thermal cauterization should be classed among radical measures.

Radical local measures include curettage, cauterization by heat, excision of the lesion with the thermocautery, and dissection excision. While each of these methods of treatment has its advocates it is difficult to decide among them.

Remembering that tubercles may be found at some distance from the apparent edge of the lesion, we can mention curettage only to condemn it. The procedure should never be used. It is more apt to spread than to cure the lesion.

Theoretically, dissection excision should give the best results, provided, of course, that the dissection can be carried on entirely in healthy tissue. This is often difficult. The depth of the lesions is at times considerable and the anatomical arrangement of the parts makes a wide excision often impossible without serious mutilation of surrounding structures. It is this limited operative field which has been responsible for the dissection in so many cases passing through active infective tuberculous material. That such material has been entered is shown by the local recurrence and the frequency with which an operative interference has been followed by a diffuse general miliary tuberculosis. Operation upon tuberculosis of this region of the body (perineum) seems particularly prone to disseminate the disease. This may be due to the close proximity and almost invariable simultaneous involvement of mucous membrane in the tuberculous process. Elting[31] has reported 9 cases of tuberculous fistula in ano, 4 of whom died subsequent to operation from a progression of their pulmonary tuberculosis. Similar untoward results are at times seen in tuberculosis of other mucous membranes. Thus Shepherd[94] has reported a case of tuberculosis of the tongue which after removal developed an acute general miliary tuberculosis rapidly terminating in death. Quénu and Hartman,[83] however, prefer dissection excision to cautery excision in tuberculosis about the perineum.*

Thermocauterization if carried sufficiently deeply should not only eradicate the lesion, but also seal off the lymphatics so that dissemination cannot occur. Its use is, however, limited by the proximity of surrounding important structures. Superficial cauterization is valueless. Only deep and thorough cauterization is sufficient. This will, unfortunately, leave a large area to heal by granulation.

Excision with the cautery knife seems to be the method of choice, even though destruction of tissue be large. By this method the exact limit of the areas to be excised can be determined and adhered to. Less destruction of contiguous parts will take place with a thin cautery blade than with a blunt cautery point.

If inguinal lymph glands are evidently infected, they should be removed. Dissection *en bloc*, as for an epithelioma of the vulva, is unnecessary. In the absence of evident involvement the lymph glands need not be removed. This is in accordance with the current view of the analogous problem in tuberculosis of the mammary gland.

* It is never certain that any operative procedure on an apparently local tuberculous focus will not activate some other known or unknown tuberculous lesion in the body. This is not only true of tuberculosis involving mucous membranes as above mentioned but also of other parts of the body. Powers[81] has reported a case of tuberculosis of the breast which after operation died of a pulmonary tuberculosis. Ill[52] and others have reported similar results in dealing with tuberculous kidneys, etc., and the list might be indefinitely multiplied.

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THE OPERATION OF CRANIAL DECOMPRESSION.

By WILLIAM SHARPE, M.D.,

HEAD OF THE DEPARTMENT OF NEUROLOGICAL SURGERY, NEW YORK POLYCLINIC MEDICAL SCHOOL AND HOSPITAL, NEW YORK CITY.

THERE are few operations in surgery having the wide application and immediate beneficial results as cranial decompression, particularly the subtemporal method. It is an operation that has been much neglected in the past, and one that is capable of still greater usefulness in the future. It is a comparatively simple operation, requiring no special technique and no special training other than a thorough knowledge of the anatomy of the temporal region and the avoidance of operative complications; if, however, difficulties are encountered then the use of the best methods for controlling them must be known. Naturally, careful hemostasis is a most important factor in obtaining good results in all cranial operations as well as due respect and regard for the delicate nerve cells of the cerebral cortex by the avoidance of unecessary and rough manipulation and digital examination; and, also, of the greatest importance, a strict asepsis.

Cranial decompressions have been limited in the past chiefly to the relief of intracranial pressure in cases of unlocalized cerebral tumor and in cases of fracture of the skull showing signs of medullary compression; the operation was performed not only to lessen the danger of a medullary edema but to avoid a secondary optic atrophy—so commonly observed in tumors of the brain. In these latter cases the site of the decompression was most frequently over the parietal area or the upper temporal region, and thus, as the tumor enlarged, the increasing intracranial pressure forced the underlying cerebral tissue through the bony opening, producing herniæ cerebri of tremendous sizes—the bane of cranial surgery. Fungi cerebri were also a common result of such protrusions. Not only was this complication to be feared, but operative damage to the underlying motor area with resulting paralysis of the opposite side of the body was always risked; besides, the intracranial pressure in cases of fracture of the skull as well as in tumors of the brain frequently produced a motor impairment by forcing the motor area upward through the bony ring of this decompression.

The reason for these complications is obvious. To remove an area of either parietal bone, not only may the underlying motor cortex be impaired at the time of the operation, but also subsequently by its protrusion upward through the bony opening. This is made possible by the extremely weak protection afforded by the scalp overlying the parietal bone; other than the cutaneous tissues in this area there is only the epicranial aponeurosis, so that

even a moderate degree of intracranial pressure is sufficient to cause a hernial protrusion. If the decompression is performed in the parietotemporal area the cranial origin of the temporal muscle to the parietal crest must be destroyed, and thus the possible protection of the temporal muscle is lost.

In contrast to these methods of cranial decompression the subtemporal route offers an almost ideal operation for intracranial conditions, requiring either a relief of the increased pressure or an exploratory procedure; not only is the underlying cortex a part of the temporosphenoidal lobe (which is a comparatively "silent" area of the brain), but the removal of the squamous bone is technically less difficult, in that it is the thinnest part of the vault of the

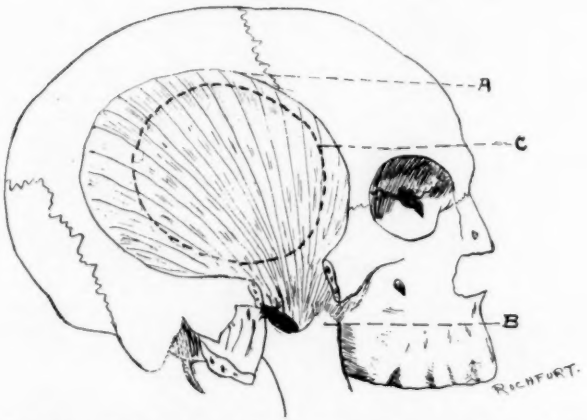

FIG. 1.—Anatomical relations of the subtemporal decompression. The temporal muscle: *A*, its origin along the parietal crest; *B*, its insertion at the coronoid process (the zygoma having been removed). The dotted line *C* shows the extent of the bony decompression opening protected by the overlying temporal muscle. The direction of the muscle fibers illustrates how easy it is to separate them longitudinally.

skull; again, the decompression opening is amply protected by the overlying temporal muscle, so that it is a rare occurrence to have a hernia cerebri following this method of cranial decompression; if the attachment of the temporal muscle to the parietal crest is carefully preserved, then it is practically impossible for a marked protrusion to occur (Fig. 1). In my opinion this method of cranial decompression should be the one always to be employed, and in this article when the word "decompression" is used it is the subtemporal decompression that is meant. In subtentorial lesions affecting the cerebellum, naturally a suboccipital decompression is to be preferred; especially is this true of tumor and abscess formations in it. As the tentorium strongly separates the cerebrum from

the cerebellum, any increase of the subtentorial pressure is more effectively relieved by a suboccipital decompression than by a supratentorial operation; besides, not only may the lesion be removed at the same time, but the bony opening will be protected by a thick layer of occipital muscles, and thus a large hernia be prevented.

The purpose of the subtemporal decompression has been much enlarged during the past few years, and it seems that its usefulness is to be developed still more in the future. Although its chief function is the relief of intracranial pressure, yet it is a most valuable method of exploration. In these two divisions, practically all of the intracranial conditions for which the operation may be advisable can be classified, and the following is a brief consideration of them:

I. The Relief of Intracranial Pressure.

A. *Tumors of the Brain.*

1. Localized Tumors of the Brain.

(*a*) Large cerebral tumors: For fear the cerebral cortex would be much more extensively damaged by opening the skull directly over the tumor, it is frequently advisable in cases of high intracranial pressure first to make a subtemporal decompression on the side of the head opposite to the tumor and then to perform the osteoplastic "flap" operation to remove the tumor. In this manner not only may the tumor be enucleated with little impairment of the surrounding cortex, but in cases where the tumor is not found as localized clinically (an occurrence of only too great frequency), then the brain may be "dislocated," as it were, toward the opposite side of the head, as made possible by the decompression opening on that side, and in this manner an exploration can be conducted with but little or no injury to the surrounding cortex. This is a most important function of the decompression in facilitating the removal of large cerebral tumors; within the past year I have removed large cerebral tumors in three cases by this method, and I am confident the operation would have ended fatally if this procedure had not been used.

(*b*) Irremovable tumors of the base and of the mid-brain: Frequently these tumors are non-malignant, the most common one being the tuberculoma; my series contains four of them. It is of the greatest importance to prevent secondary optic atrophy and its resulting blindness by an early relief of the intracranial pressure. These tumors may enlarge to a certain size, then remain stationary, become smaller, and even disappear clinically, so that if blindness is prevented during their stage of active growth, then an excellent result may be obtained. If the tumor should continue to grow, then the headaches and blindness may be delayed for months until the last stage of the condition.

2. *Unlocalized Tumors.* In the hope that the tumor may localize itself clinically and thus permit of its removal, and yet to prevent the secondary optic atrophy resulting from the increased pressure

of its growth, it is advisable to perform an early decompression and, if necessary, a bilateral decompression. During the past year I have treated five cases in this manner; it is surprising to observe the improvement in such cases; a cessation of headache, nausea and vomiting, the rapid subsidence of the beginning "choked disk" —the forerunner of secondary optic atrophy and blindness. No case of high intracranial pressure producing "choked disks" should be permitted to remain weeks while a definite diagnosis is being made without a relief of that pressure by a decompression; only too frequently such cases are brought to the surgeon after blindness has occurred, and once an advanced degree of secondary optic atrophy has supervened there is little if any recovery of sight. Not only will an early decompression delay and even prevent blindness in these cases, but in will prolong the life of the patient by lessening the medullary compression, and thus the unlocalizable tumor may extend into a part of the brain producing unmistakable signs of its situation, so that the tumor can be successfully removed. This is the common history of tumors of the frontal and temporosphenoidal lobes, especially of the right cerebral hemisphere; as tumors of the frontal lobe extend posteriorly to the motor area then a motor impairment of the opposite side of the body appears, and if downward upon the optic nerve, then an ipsolateral primary optic atrophy results; motor aphasia frequently appears as tumors of the left frontal lobe extend backward into the motor speech area; in tumors of the temporosphenoidal lobe a similar motor impairment occurs if the lesion extends upward into the motor tracts or forward into the motor speech area.

In similar cases of suspected tumors of the frontal or parietal lobes, and if the intracranial pressure is not extremely high, it is advisable to perform an osteoplastic "flap" operation first, and if the tumor is not found or after its removal the brain is still under marked tension, then a subtemporal decompression can be performed by rongeuring away the squamous portion of the temporal bone and the lower portion of the bone flap itself; in this manner another scalp incision is avoided.

B. *Fractures of the Skull.* Whether the fracture is of the vault or of the base a decompression is advisable only when the fracture is associated with high intracranial pressure; naturally the palliative expectant treatment of absolute rest and quiet, an ice-bag to the head, catharsis and liquid diet, are usually sufficient for those cases of fracture of the skull showing no marked signs of intracranial pressure; that is, a fracture of the skull is not an indication for an operation unless there are definite signs of an increase in the intracranial pressure. An ophthalmoscopical examination of the fundi of the eyes is the most reliable and accurate means of determining an increase of the intracranial pressure, whether this increase is due to a swollen edematous brain, a depressed fracture of the

vault, or to an intracranial hemorrhage of extradural, subdural or intracerebral origin with cerebral lacerations. It is not so essential to remove the depressed area of bone or the intracranial clot as it is to offset the pressure effects of the depression or clot upon the cerebral cortex; naturally, in depressed fractures of the vault, the depressed area should be elevated or even rongeured away, and in cases of intracranial hemorrhage, the clot should be removed, but in many cases, even when their removal is possible, the intracranial pressure still remains high and it is this continued increase of intracranial pressure which damages the cerebral cortex and produces the impairment—both physical and mental. It is not so much a question of fracture of the skull as the effects upon the brain of the injury producing the fracture; in many cases a fracture of the skull is not present and yet a cortical hemorrhage and even cerebral lacerations may have resulted from the injury. It is in these cases of intracranial lesions resulting from injuries to the head and showing definite signs of increased intracranial pressure that an early relief of this pressure is advisable—not only to avoid the danger of a medullary compression and its possible collapse, and therefore the death of the patient, but to lessen the percentage of the post-traumatic conditions so common in these cases, such as persistent headaches, dizziness, changed personalities varying from the depressed state to a highly irritable condition, generally nervous instability, and even epilepsy in its different forms. A decompression should only be advised when there are marked signs of intracranial pressure as revealed by the ophthalmoscope. Signs of medullary compression, such as a retarded pulse, a slow and irregular respiration of the Cheyne-Stokes type, and a high blood-pressure are rather late signs of intracranial pressure, and if the patient is allowed to reach this dangerous condition, then it is doubtful if the patient will recover—operation or no operation; a medullary edema and collapse of the patient may occur at any moment.

1. Fractures of the Vault.

(*a*) Linear fractures with no depression of the fragments: In these cases a decompression should be performed if the intracranial pressure is high. It has been rare in my experience for fractures of the vault, unless small locally depressed ones, to be limited to the vault alone; usually the "crack" extends downward to the base—the thinnest and weakest part of the skull. However, this type of fracture, as revealed by the Roentgen-ray, frequently shows no sign of intracranial pressure, and therefore an operation should not be considered.

(*b*) Depressed fractures of the vault should always be elevated. If this is impossible, then it is usually wiser to remove the depressed fragments, whether the intracranial pressure is high or not. The danger of local damage to the underlying cortex with the subsequent

formation of adhesions, etc., rendering the cerebral cortex unstable and thus subjecting the patient to the frightful risk of epilepsy, is a calamity always to be feared, and especially in depressed fractures of the vault. If the intracranial pressure is high, then it is wiser to perform a subtemporal decompression on the same side of the head as the depressed area, and in this manner the general intracranial pressure is relieved. If the depressed area overlies either motor tract of the cerebral cortex, and the intracranial pressure is very high, causing a double papilledema, then it is advisable to perform the subtemporal decompression first and thus relieve the pressure, so that there will be less danger of injury to the motor tract when the depressed area is elevated or removed; otherwise the intracranial pressure may be so extreme as to force cerebral tissue through the fractured opening of the vault and a motor impairment of the other side of the body result.

2. Fractures of the Base. These cases should be treated by the expectant palliative method; however, if the signs of high intracranial pressure appear then an early decompression will not only save a larger percentage of patients than the other method of treatment, but it will lessen the number of post-traumatic conditions. In this connection it may be interesting to note that of the total number of 77 cases of fracture of the skull which were admitted during the year ending June 1, 1914, to the department of neurological surgery of the New York Polyclinic Hospital, 27 of them died; that is, a mortality of 35.06 per cent. Of these 27 cases, however, 20 of them were moribund upon admission—11 of them dying within a few minutes to two hours after admission, and the remaining 9 dying within six to twelve hours after admission; 36 cases of the 77 admitted were operated upon, with a mortality of 9 cases following operation; that is, an operative mortality of 25 per cent.; however, 4 of them revealed at autopsy subtentorial fractures with hemorrhage—a most dangerous condition, as it causes direct pressure upon the medulla; 2 died, nine and sixteen days respectively following the operation, from meningitis due to infected hematomata of the scalp; 1 died on the twelfth day postoperative from pneumonia—the patient being seventy-five years of age—and the ninth case died on the sixth day postoperative from a meningitis, probably due to a "slip" in the operative technique. Naturally the cases operated upon were the severe cases showing signs of high intracranial pressure. It is a mistake to operate upon these cases when in a condition of severe shock; it is better to wait several hours until the shock has been overcome, otherwise the operation is but an added shock.

C. *Brain Abscess, Particularly of Either Temporosphenoidal Lobe.* The accurate diagnosis of brain abscess is a most difficult one, and any operative procedure should always be conducted as an exploratory operation. As a rule, abscess of the cerebellum is

diagnosed with less difficulty than abscess of either temporosphenoidal lobe or of either frontal lobe; therefore if an abscess of the cerebellum can be excluded in a case with the usual history of previous otitis media it is much wiser to perform a subtemporal decompression over the suspected temporosphenoidal lobe and thus be enabled not only to relieve the intracranial pressure (if present), due to the abscess, but to permit a careful exploration of the entire temporosphenoidal lobe through a non-infected area; if the abscess is found, then free drainage is afforded through the lower angle of the split temporal muscle, and the decompression will offset the pressure effects of the swollen edematous brain resulting from the exploratory punctures and the presence of the abscess itself; again a meningitis is much less liable to occur with free drainage and a lowered intracranial pressure than if the intracranial pressure were high enough to lessen the resistance of the tissues to an infective meningo-encephalitis; if the abscess should not be found then a relief of the intracranial pressure has been obtained and no harm done; the abscess may localize itself later. It is a dangerous procedure to puncture the dura blindly or open it through an infected area such as the mastoid; if the abscess is not found the danger of infection is great indeed; and if it is found the resulting cerebral edema can not be lessened by the small operative opening, so that the danger of a medullary compression is a serious menace; in my opinion, patients die not so much from the presence of the abscess, but rather from the cerebral edema with its resulting medullary compression.

Within the past year I have operated upon two cases of abscess situated in the anterior median portion of the left temporosphenoidal lobe, and if I had not used the subtemporal decompression I am confident I should have overlooked them. Again, in cases of suspected brain abscess it is much better to perform an early exploratory operation than to wait until the patient shows marked signs of medullary compression; the danger of the abscess rupturing into either the subdural space or the ventricle is then much greater.

My own series of operated cases of brain abscess is limited to 10. Of these 4 died: 2 from medullary edema resulting from a too small opening of the occiput in cerebellar abscess; 1 from a meningitis following the drainage of a left frontal abscess through a small opening—no decompression having been performed; and the fourth one died from a large temporosphenoidal abscess—three to three and a half inches in diameter—which gnawed its way into the ventricle after a decompression with free drainage had been established. The remaining 6 cases recovered; 4 were situated in the temporosphenoidal lobes, and each one was drained through a subtemporal decompression; 1 a cerebellar and 1 a right frontal abscess—the latter case having a decompression performed until the abscess located itself clinically seven weeks later.

D. *Cerebral Spastic Paralysis.* Selected cases due to an intracranial hemorrhage at birth. Attention has been centred in the past upon the correction of deformities and the lessening of spasticity; the improvement following these operations has been only temporary in all but the mild cases. Naturally the cases of spastic paralysis due to a lack of development or malformation of the brain and its pyramidal tracts are not operated upon and could not be benefited by any cranial operation, but only those cases of cerebral spastic paralysis having a history of difficult labor with or without instruments, and upon ophthalmoscopical examination of the fundi, the definite signs of intracranial pressure are to be observed in the dilated retinal veins, edematous blurring, and haziness of the nasal halves of the optic disks and the more marked signs of old intracranial pressure—these are the cases that can be improved by merely a relief of the intracranial pressure; the local pressure effects of a hemorrhage or of its resulting cystic formation are offset by the decompression, and if the intracranial pressure is high then a bilateral decompression may be performed. If the hemorrhagic clot or its subsequent cyst can be removed, so much the better; but this is not possible in many cases. Naturally the longer the clot and its cystic formation are allowed to exert pressure upon the cortex the more impaired do the nerve cells of the cortex become; in my experience of 65 operated cases, however, only 5 of them revealed the hemorrhagic cyst in or beneath the cortex; that is, the cortical nerve cells were not primarily destroyed but merely impaired by the pressure of the clot and its cyst upon them, as was the condition in 45 cases observed at the operation; thus the longer the condition of intracranial pressure is allowed to continue, just so much more will be the impairment of the cortical nerve cells, resulting in a persistent and even increasing stiffness and spasticity, and a steady mental deterioration in the majority of cases. Most of my cases have been from five to eight years of age—the youngest six months and the oldest twenty-one years of age; the older the patient above twelve years of age the less was the improvement; but even the older ones are improving. The operative mortality has been 6 cases; 4 of these, however, were extreme cases of spastic diplegia under two years of age, very much emaciated and having great difficulty to breathe or to swallow; this type of case should not be operated upon, as the anesthetization alone is too great a risk. However, no case of spastic paralysis, no matter how extreme, should ever be operated upon unless there are definite signs of intracranial pressure as shown by a careful ophthalmoscopical examination; in this manner the spastic cases due to a lack of development and malformation of the brain and its tracts are easily excluded and should never be operated upon, as their condition could not possibly be improved by a cranial operation. Naturally, sufficient time has not yet elapsed since the first operation

(June, 1913) to establish the permanency of the improvement in these selected cases of spastic paralysis, but from pathology of the condition we see no reason why the children should not continue to improve as they are doing. A report in detail is to be published soon.

II. As an Exploratory Procedure.

This is particularly true of suspected lesions of either temporosphenoidal lobe, the lower portion of either motor area, the posterior lower portion of either frontal lobe, and the motor speech areas. It is a much more simple operation technically than the osteoplastic "flap" operation, requiring half the time, and the bony opening can be firmly covered by the temporal muscle so that no deformity results. Again, if an increase of the intracranial pressure is found at operation then the decompression will relieve it.

Besides the cranial conditions selected above as being benefited by the operation of subtemporal decompression, there are other intracranial lesions for which the decompression may be used; but this work is now in its experimental stage, and will be discussed later.

Not only will a decompression itself relieve the increased pressure, but a tapping of the lateral ventricle may be easily performed through the decompression opening by means of a small blunt cannula, and in this manner the presence or the absence of a dilatation of the ventricles is ascertained—a most important aid in ascertaining the location of the intracranial lesion; besides, the ventricular tapping will greatly relieve the intracranial pressure—at least temporarily.

The Technique of the Subtemporal Decompression. There should be the usual preparation of the patient for an operation. The side of the head selected for operation is carefully shaved, either on the preceding night and a green soap poultice applied, or in emergency cases the operative site is closely shaved just before the operation. Unless there are clinical signs indicating a lesion of the left hemisphere the decompression is always performed on the right side in order to avoid the motor speech area, which is situated in right-handed persons in the posterior portion of the third left frontal convolution, and *vice versa* in left-handed patients. The patient is placed upon his back with his right shoulder elevated by a sand-bag, so that the right side of the head can be more easily made parallel to the table; in this manner the operative site is well exposed and it does not compel the operator, standing at the head of the table, and his assistants to assume tiring positions. The anesthetist is seated under a sheet at the waist of the patient, and in this way he is entirely excluded from the field of operation. The anesthesia in these cases requires the most skilful administration; especially is this true to avoid an extreme cyanosis and congestion not only during the induction of narcosis, but after the

dura has been incised and the cerebral cortex exposed; coughing or even labored respirations at this stage of the operation may result disastrously by forcing the cortex through the bony opening; the cortex may be ruptured and serious hemorrhage occur. Dr. Charles S. Hunt, who has administered the anesthetic in all of my cases, uses a mixture of ether and oxygen most successfully; he has found it necessary to deepen the narcosis just before the dura is incised, otherwise the sudden relief of intracranial pressure will allow the patient to show signs of consciousness by coughing, etc.—a complication to be feared at this stage of the operation.

The side of the head and face are now carefully "scrubbed" with green soap and water for five minutes, and then alcohol is sponged over the operative area. Iodin is only used in emergency cases when the scalp can not be thoroughly prepared; it tends to irritate the skin in many cases and thus render a secondary infection possible. A superficial incision in the skin is now made to indicate the area of the operation, and then towels wet in a 1 to 3000 solution of bichloride are clipped to the scalp at each side of this incision; in this manner the head is completely covered and the towels can not become disarranged, so that there is little danger of infection.

By using the method of pressure-traction at each side of the incision and the forefinger of the assistant to compress the temporal artery as it passes over the zygoma, the incision can be made with little loss of blood—a most important factor in all cranial operations; a cranial tourniquet cannot be used in this operation, and the other methods for controlling hemorrhage of the scalp, such as deep sutures, clipping of the scalp, etc., are time-consuming, troublesome, and even dangerous by increasing the risk of infection; besides they are ineffective in many cases.

The incision itself is made vertically upward through the scalp from a point just above the zygoma and one-half inch anterior to the external auditory meatus to the middle of the parietal crest, and thus overlying the origin of the temporal muscle; it is about three to three and a half inches in length, and is parallel to the fibers of the underlying temporal muscle (Fig. 2). Small curved hemostats are used to compress the branches of the temporal artery, and then the temporal fascia is incised vertically and the fibers of the temporal muscle are split longitudinally and retracted, exposing the squamous portion of the temporal bone. A sharp periosteal elevator is used to separate the muscle from the underlying bone; great care should be taken not to destroy the attachment of the muscle and its fascia to the parietal crest—otherwise the closure of the temporal muscle will be greatly weakened.

The Doyen perforator and burr are now employed to make a small opening at the lower angle of the operative area—that is, the thinnest portion of the squamous bone (Fig. 3). Small rongeurs enlarge the opening until it is possible to use a larger rongeur having

one blade bevelled and flattened so that it can be easily inserted between the dura and bone; frequent explorations and removal of adhesions between dura and bone with the dural separator will prevent the dura from being torn. In this manner a circular opening as large as possible under the temporal muscle is made—extending from the base of the skull up to the parietal crest and having a diameter of two and a half to three inches.

Before opening the dura it is important that all oozing from the bony margins should be stopped; the best method for controlling this bleeding from the diplöe and its sinuses is the rubbing of a

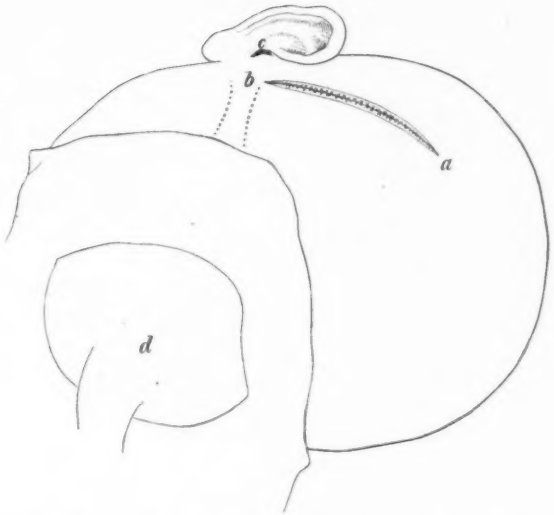

FIG. 2.—The superficial incision *a–b* shows the vertical extent of the operation—two and one-half to three inches; *a*, the middle of the parietal crest; *b*, the zygomatic arch; *c*, the external auditory meatus; *d*, the ether-oxygen apparatus in position.

bone-wax into the edge of the bone, and it is surprising how quickly this troublesome complication is overcome. Dr. Norman Sharpe has formulated a bone-wax which is most effective; its composition is as follows: white wax, 7 parts; almond oil, 2 parts; salicylic acid, 1 part. It should be kept in a 5 per cent. solution of carbolic acid. This wax may be sterilized before each operation and then allowed to cool so that it hardens and is easily moulded; small pellets, the size of peas, are then applied to the oozing bone. It is an effective method of plugging the middle meningeal artery when it channels the bone; it seems to me that it might be used in operations upon bone elsewhere—such as the mastoid, resections

of bone, etc. It is far superior to the old method of using wooden pegs in cranial surgery. In fractures of the skull the middle meningeal artery is frequently torn in the subtemporal area, so that it is a simple matter to remove the clot and then plug the bleeding point with the wax.

FIG. 3.—The temporal muscle retracted. Using the Doyen perforator *a* to open the skull at the lower angle of the incision, that is, at the thinnest part of the squamous portion of the temporal bone. The Doyen burr *b* is next used to enlarge this opening so that rongeurs may be employed.

The dura is now incised by carefully cutting through its outer layer first with a sharp knife; elevating the dura from the underlying cortex by means of the small dural hook inserted into its outer layer, the inner layer can now be safely incised until a small pinpoint opening is made; a grooved director bent at right angles may

now be carefully inserted and the dural opening enlarged by cutting the dura upon the director (Fig. 4). When the dural incision is about one inch in length, I have found it easier and quicker to insert a spoon-shaped spatula and then cut the dura with a sharp pair of scissors; this method is not only safer, but it allows the incision to approach the dural vessels as closely as possible, so that these vessels may be clamped before being cut. Not only is it time-consuming and troublesome to ligate the dural vessels with silk or catgut, but it is dangerous to insert a needle beneath the vessels

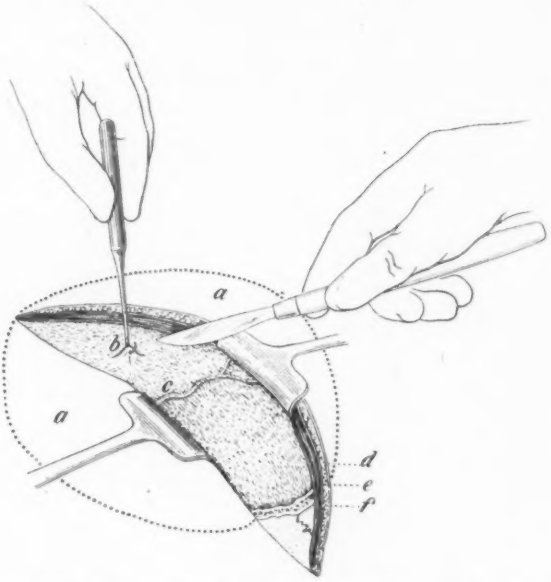

FIG. 4.—Dotted lines *a* show area of bone (two and one-half by three inches) removed. Incising the dura which is elevated from the underlying cortex by the dural hook *b*; *c*, middle meningeal artery; *d*, skin; *e*, temporal fascia; *f*, temporal muscle.

before the dura has been incised for fear of puncturing one of the many cortical vessels lying beneath and thus complicating the operation; if the decompression is to be performed it should at least not injure the brain. An excellent method of dealing with the dural vessels is the application to them of the small silver V-shaped clips used by Dr. Harvey Cushing, and then the dura and its vessel may be safely cut between each pair of clips and no bleeding result; these clips may be left on the vessels, and I have never seen any ill-effects occur; in three cases at autopsy within two years after

operation, the clips were found *in situ;* no tissue reaction had occurred, so that they are apparently not irritating foreign bodies; in some cases where the dura was very vascular I have used as many as eight clips. The clips are made by snugly wrapping German silver wire No. 24 around a rectangular rod and then bisecting the roll; V-shaped clips are thus formed, and after sterilization these can be put in a clip holder (similar to a hemostat with a grooved end) and slipped upon the dural vessel. This method saves much time and entails no risks.

The dural opening is thus enlarged in a crucial or stellate manner until the bony margins of the decompression are reached. It is important to incise the dura downward to the base of the skull so that the middle fossa of the skull can be easily and freely drained—so essential in all fractures of the skull with edematous, swollen brains with or without hemorrhage. Through this opening any underlying pathological lesion can be dealt with freely and safely; subdural clots may be removed in fractures of the skull; tumors enucleated and abscesses drained. Aided by the spoon-shaped spatula and a good electric head-light, the neighboring areas of the frontal lobe, the parietal lobe, and the posterior portion of the temporal lobe may be accurately explored for any cortical lesion. If the cerebral tension is high then the ipsolateral ventricle may be drained by the ventricle puncture needle; all parts of the temporosphenoidal lobe and even the posterior portion of the frontal lobe and the lower portion of the parietal lobe can be accurately explored in this manner in cases of suspected sub-cortical lesions, as tumors and abscess.

After the cerebral lesion has been removed or drained, or if merely the relief of intracranial pressure is desired, then a rubber tissue one-quarter inch in width and several layers in thickness is inserted at the lower angle of the wound and inside the dura beneath the temporosphenoidal lobe as far as possible; in this manner excellent drainage is afforded the middle cranial fossa. Before closure of the opening it is important that there should not remain any bleeding-points—no matter how small; small cotton pledgets wet in warm saline solution are frequently sufficient in many cases of cortical oozing, or a small piece of the temporal muscle applied to the bleeding point and then compressed for a few seconds will stop a most troublesome oozing. When tumors are removed, then packs of cotton wet in warm saline solution and pressed for a few moments into the cavity of the enucleated tumor mass will quickly prevent a large hemorrhage; it is rarely necessary to leave packing intracranially.

The drain having been inserted beneath the temporosphenoidal lobe the temporal muscle is now sutured with interrupted fine black silk—usually in two layers (Fig. 5); then the temporal fascia and finally the subcutaneous tissues; the vessels of the scalp are not

ligated as the mere suturing of the subcutaneous tissue is sufficient to compress their vessels; at times, however, the temporal artery

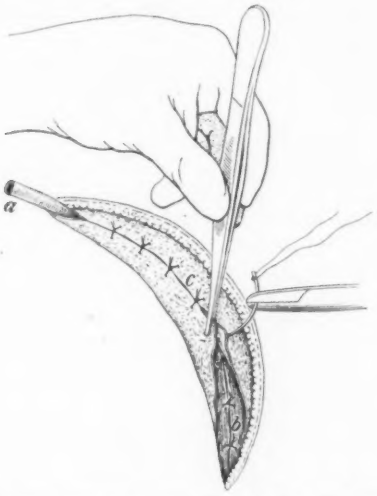

FIG. 5.—Rubber tissue drain *a* inserted into middle fossa beneath the temporosphenoidal lobe and passing out at lower angle of incision; *b*, fibers of temporal muscle reunited by layers of interrupted fine silk sutures; *c*, temporal fascia being sutured by interrupted fine silk.

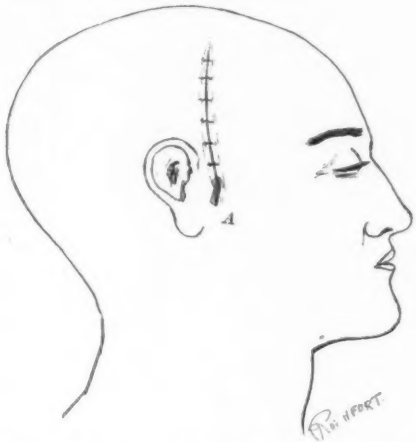

FIG. 6.—Skin sutured with fine silk. All towels removed. *A*, drain of rubber tissue.

itself is ligated. The skin is carefully approximated by fine black silk (Fig. 6). Dry gauze pads are now applied to the operative

area, and after a cotton pad well covered with sterile vaselin is placed behind the lobe of the ear to prevent its being pressed against the skull and causing severe pain, the usual bandage of roller gauze is used and held in place by several strips of adhesive plaster (Fig. 7).

In operations of subtemporal decompression the dural opening is never sutured together; in the first place, if there is much intradural pressure, it would be impossible to approximate its edges, and secondly, to suture the dura would be to destroy the object of the decompression—the relief of intracranial pressure; for in adults the dura is inelastic, so that there can be no real decompression if the dura is unopened or sutured after being opened. There

FIG. 7.—Dressings applied and held by bandage of roller gauze. A small pad of cotton and sterile vaseline is placed behind the lobe of the ear to prevent pain from its pressure against the bony skull; opposite ear left uncovered. Small strips of adhesive plaster used to hold bandage firmly.

is no danger apparently in leaving the dura opened; adhesions do not form, and in three cases at autopsy, two of them revealed the formation of an entirely new dura. The overlying temporal muscle forms a safe protecting covering.

The postoperative treatment consists of a moderate elevation of the head and shoulders, with the administration of hot saline solution per rectum every four hours for the first day; if much operative shock is present, then hot black coffee per rectum may be given immediately after the operation. The patient should be quiet—morphin or codein being used if necessary. Water may be given by mouth as soon as the nausea ceases, and liquids on the following day; soft diet on the fourth day.

At the first dressing on the second day, the drain is removed and possibly one-third of the skin sutures. At the second dressing on the fifth or sixth day postoperative, all sutures are removed and the patient may now have a light diet. In uncomplicated cases the patient may leave the hospital on the tenth day postoperative. It is surprising how quickly patients recuperate from the operation—there being, as a rule, little if any shock.

The advantages of the subtemporal route over other methods of cranial decompression are chiefly due to its anatomical relations. Not only is the squamous bone underlying the temporal muscle the thinnest part of the vault of the skull and therefore less difficult to remove, but it exposes a part of the brain most frequently involved in cases of fracture of the skull where the middle meningeal artery is torn or the temporosphenoidal lobe is lacerated; in cases of abscess of the temporosphenoidal lobe following its usual cause an otitis media. With little difficulty the lower portion of the motor tract may be explored as well as the posterior portion of the frontal lobe, and on the left side the motor speech area is easily observed. Another important advantage is the fact that the part of the brain lying directly beneath the decompression opening is the cortex of the temporosphenoidal lobe—a comparatively silent area of the brain; for this reason any possible operative damage is not revealed clinically, and in cases of high intracranial pressure the protrusion of this part of the brain into the decompression opening does not produce paralysis, etc.—a frightful result of decompressions performed in the parietal area. That is, a subtemporal decompression relieves increased intracranial pressure without cerebral impairment. Besides it affords excellent drainage for the middle fossa of the skull at its lowest point—an important consideration in cases of fracture of the skull.

Again, the thick overlying temporal muscle not only makes possible a firm closure but also allows the underlying bone to be removed so that a permanent decompression results with no danger of a hernia cerebri. The scalp is not weakened by draining through the split temporal muscle and no unsightly protrusion occurs; the scar is always inside the hair-line. In men the rim of the derby or straw hat affords some protection to the area of the decompression, although no protection is really necessary, as the temporal muscle is thick and thus the underlying cortex is well protected; besides the cortex itself is comparatively a silent area of the brain, so that even if it were injured by an object being thrust into the opening, no clinical signs would appear unless a large cortical vessel were torn.

The vertical incision of the scalp in this operation is far superior to the older method of a curvilinear incision over the parietal crest. Not only may the pressure-traction method of hemostasis be used much more effectively with the vertical incision, but the

temporal artery is clamped at its lowest point and before it ramifies into numerous smaller vessels, whereas in the curved incision the many branches of the temporal artery are severed individually and each one must be clamped separately; again, it is easier to enlarge the bony opening downward to the base of the skull when the vertical incision is used—an important point for drainage in cases of fracture of the skull. To preserve the strong attachment of the temporal muscle to the parietal crest is difficult and even impossible when the usual curved incision is used; in this manner the decompression may so weaken the side of the head that a hernia cerebri appears as the intracranial pressure increases; especially is this true in irremovable tumors of the brain; this complication is a most rare occurrence following a decompression performed with the vertical incision and a careful regard for the attachment of the temporal muscle.

Conclusions. The operation of cranial decompression is one that should be used much more frequently than it is at present; especially is this true in the conditions of brain tumor, fracture of the skull, brain abscess, and selected cases of spastic paralysis due to an intracranial hemorrhage at birth.

The subtemporal method of cranial decompression is the ideal route; besides being less difficult technically it exposes an area of the brain most frequently involved. This permanent decompression opening does not weaken the skull in that the thick overlying temporal muscle protects it most adequately, so that herniæ cerebri are not to be feared.

The operative mortality is low. Patients with intracranial conditions should not be permitted to become blind or to reach the dangerous stage of medullary compression without a subtemporal decompression being performed early.

FRACTURE OF THE BASE OF THE SKULL WITH ESCAPE OF CEREBROSPINAL FLUID FROM THE EAR. THE EFFECT OF ATROPINE AND EPINEPHRIN UPON THE SECRETION.[1]

By J. Walker Moore, M.D.,
LOUISVILLE, KENTUCKY.

The purpose of this paper is threefold:

1. To report a case of fracture of the base of the skull with the escape of an unusual amount of cerebrospinal fluid from the ear.

[1] I have to thank Dr. Charles H. Frazier most cordially in making it possible for me to carry out the work presented in this paper, and freely placing at my disposal valuable unpublished data concerning the effects of the injection of certain saline extracts of the body organs upon the secretion of cerebrospinal fluid in dogs.

2. To outline briefly the evolution of the hypothesis that the cerebrospinal fluid is a true secretion.

3. To present the effect both chemically and clinically of the hypodermic injection of atropin and epinephrin upon the secretion of cerebrospinal fluid.

Fracture of the base of the skull with the escape of cerebrospinal fluid from the cranium has been observed for centuries. Bidloo the elder (quoted by St. Clair Thomson), writing in the latter half of the seventeenth century, reported a case of a patient who had a fracture of the bridge of the nose followed by a continuous flow of clear watery fluid from the right nostril; twenty ounces of this fluid escaped in twenty-four hours. Stalpartius von der Wiel, in 1725, published a case in which a large quantity of clear watery fluid escaped from the ear after a severe injury to the head. Matthein and others have collected a number of such cases. Indeed, judging from the recent literature, surgeons do not look upon this as a matter of rare occurrence.

The case which we have to report is not a unique one by any means, however, judging from his age, weight, and stature; the amount of cerebrospinal fluid that escaped from the ear at regular intervals is rather remarkable.

Case I.—W. R., Episcopal Hospital, aged six years, male; weight thirty-five pounds.

Eighteen hours before admission into the hospital the child fell down a flight of stairs backward while attempting to catch a ball that he had thrown upward. The screams attracted the mother's attention. She found the child lying on the floor, in an unconscious condition, bleeding from the left ear. Within a few minutes blood and clear colored fluid flowed alternately from the left ear. Later (about twenty minutes) the blood ceased entirely, but the clear colored fluid continued to flow, with occasional momentary stoppage up to the time of admission into the hospital. The child remained unconscious for six hours after the accident; thereafter was conscious of things around him. He vomited just after the fall and again six hours later.

The child was of instrumental delivery. Since the age of eight months the patient has had frequent epileptic seizures, the attacks occurring at irregular intervals. The child may go as long as three days without a seizure, on the other hand the attacks may occur daily, or several times during the day, and continue in this manner for two or three days. The oncoming attack is usually ushered in by the child being peevish, fretful, restless, spitting, etc. Then comes the seizure which manifests itself by a rapid contraction of arms and legs, a sudden scream and a falling to the floor, rapidly becoming cyanotic and blue in the face. At times the child froths at the mouth but never bites his tongue. The attack is usually three minutes in duration. The child, acccording to the parents,

is bright and has a wonderful memory. No history of mental deterioration. Had a discharging right ear two weeks ago which rapidly cleared up under treatment. Mother states that the child did not have an epileptic seizure before the fall, nor were there any symptoms of an attack following the accident.

On admission to the hospital, eighteen hours after the accident, the examination revealed a fairly well-nourished child of six years, somewhat restless, but nothing more than one would expect of a child in a strange place. The child would heed immediately when his name was called, and would protrude the tongue or raise the arm when asked to; we were unable to draw the patient into a conversation, but he would at intervals articulate words, as water, mother, and the like. However, he would never utter a complete sentence.

Aside from the discharging left ear the physical examination was essentially negative. There were no signs of injury to the scalp. Eyes reacted promptly to light, pupils were equal. Ocular movements normal. Cardiac action was rapid, pulse of good tension and volume. Lungs, abdomen, and extremities were negative.

The patella, achilles, biceps, and triceps reflexes reacted promptly but were not increased. There were no palsies, no ankle-clonus. Skin reflexes and sensation normal.

Temperature, 97°; pulse, 130; respiration, 24.

From the left ear could be seen a continuous flow of clear watery fluid. The flow was so rapid that within a short time the pillow-cover in the region of the head would be soaked with the fluid. The fluid reduced Fehling's solution. Specific gravity, 1007. One c.mm. showed 1730 red blood corpuscles, 49 polymorphonuclear leukocytes, and 39 lymphocytes.

March 16. The child is quiet, lies with the right side of the head on the pillow. The left ear continues to discharge a clear watery fluid at irregular intervals; that is to say, the flow ceases an hour or more, two or three times in the twenty-four hours.

The child had a convulsion which lasted two minutes; during the convulsion the lips became cyanosed, face pinched, upper and lower extremities contracted rapidly. There was no frothing at the mouth nor biting of the tongue. Had to be catheterized. Temperature, 103; pulse, 135; respiration, 24.

March 17. Very little change in condition. The child drinks a great deal of water and takes liquid diet well.

The ear continues to discharge at irregular intervals. Had a convulsion, similar to the one on the previous day. No record was made of the amount of secretion during the convulsion, but the attending nurse states that there was not a noticeable increase during the convulsion, judging from the wet spot on the pillow cover.

March 18. The ear ceased secreting only once during the twenty-four hours, and that was for about three hours, while

the child was asleep. There is a suggestive Kernig and reflex resistance of the neck muscles to flexion of head. The right ear began to discharge mucopurulent material Secretion collected from the left ear by means of an eye dropper in sixty minutes was 15 c.c.

The eye-grounds were examined by Dr. Bromley. The report was as follows:

O. D. Nerve circumscribed and flat; very little venous congestion. Media clear.

O. S. Slight engorgement of veins, nerve perfectly flat and circumscribed. No edema of retina. Media clear.

March 19. Patient takes water and liquid nourishment freely. The fluid collected from the ear in sixty minutes amounted to 21 c.c. The child dropped off to sleep and the ear stopped secreting for hours. On awakening the ear began secreting again.

Ten grains of urotropin were given, and fluid collected every five minutes for two hours and placed in separate test-tubes. We were unable to demonstrate the presence of urotropin with the bromine water test in the fluid collected.

Blood Count. White blood corpuscles, 17,200; polynuclears, $66\frac{2}{5}$ per cent., mononuclears, 3 per cent.; transitionals, $7\frac{2}{5}$ per cent.; lymphocytes, $22\frac{1}{5}$ per cent.; eosinophiles, 1 per cent.

March 21. Very little change in condition of patient. Kernig's sign suggestive. No rigidity of neck.

March 23. Child is quiet most of the time, occasionally becoming restless. Kernig is positive. No rigidity of neck; no bowing of back.

March 24. The child is quite restless at times. There is rigidity of the neck muscles, with slight retraction of the head. Kernig's sign is positive. No bowing of the back. Pulse is rapid; secretion from left ear is scanty.

Blood Count. White blood corpuscles, 25,350; polynuclears, 79 per cent.; transitionals, 3 per cent.; lymphocytes, 18 per cent.

March 25. The patient appears to be in great agony, crying out at frequent intervals; retraction of neck is marked; there is also bowing of the back, with drawing up of lower extremities. The left ear has ceased secreting entirely. Skin is dry; eyes sunken; tongue parched; radial pulse scarcely perceptible.

From this point the patient rapidly went downward, and died March 28.

The autopsy was performed by Dr. C. Y. White, director of the pathological laboratory of the Episcopal Hospital. He reports as follows:

The dura is transparent, the inner surface being smooth and glistening. The vessels of the pia mater are only slightly congested. No macroscopic evidence of a meningitis. No edema beneath the pia.

On severing the brain from the cord an excessive amount of cerebrospinal fluid escaped into the base of the skull.

The dura is entirely stripped for the purpose of examining the skull, and there is found a fracture involving the squamous and anterior surface of the petrous portion of the left temporal bone. That part of the fracture involving the petrous portion is Y-shape, and extends into the internal auditory meatus. One limb of the Y begins with the depression for the Gasserian ganglion; the other with the opening for the small petrosal nerve. The two uniting just external to the Hiatus Fallopii and running outward parallel with and $\frac{1}{8}$ of an inch beneath the superior border to the squamous portion, where it continues directly upward in that bone for one inch.

Figure showing the Y-shaped fracture involving the petrous portion of the left temoral bone. The fracture was outlined with lead pencil and a photograph taken of the bone of skull.

Dr. W. B. Cadwalader made numerous sections of the brain and choroid plexus, and submits the following report:

Sections were made from various parts of the cerebral cortex and the cerebellum. For the most part they were entirely negative, but here and there in some sections a few polymorphonuclear leukocytes could be seen infiltrating the pia, and grouped about some of the smaller bloodvessels within the fissures of the cortex. This was a real meningitis, yet it was so slight that it would require more than a superficial examination to find it. Sections from the basal ganglia, internal capsule, pons cerebellum, and different levels of the spinal cord appear to be entirely normal. There were no evidences of meningitis in these parts and the tissue stained

normally with the Weigert stain. Sections of the choroid plexus were made and were stained by a number of different methods. All the cells appeared entirely normal. I could not demonstrate some of the granules which are thought to react differently to stains, and which have been supposed to have some relationship to secretory functions. Comparing the sections taken from this case with similar sections of two other brains which ought not to have had any disease of the choroid plexus, I could not really find any difference. On the whole it is just to conclude that this specimen, brain and cord, shows absolutely nothing abnormal except a very mild and diffuse infiltration of the pia which was probable of recent origin.

THE EVOLUTION OF THE HYPOTHESIS THAT THE CEREBROSPINAL FLUID IS A TRUE SECRETION. The hypothesis that the cerebrospinal fluid is a secretory product of the choroid plexus has been the source of infinite research for a number of decades. Leonard Hill,[2] in the early 90's, advocated the hypothesis that the fluid is a serous transudation from the capillaries of the vascular choroid. He regards the cerebrospinal fluid as the lymph of the brain, its secretion and resorption being explained on the same lines as other lymphatic exudate. He contends that the secretion of the fluid increases with the rise in cerebral capillary pressure and the latter varies directly and absolutely with vena cava pressure. He cites a case of St. Clair Thomson's in which there was a continuous flow of cerebrospinal fluid from the left nostril. At the invitation of St. Clair Thomson[3] he made the following observations:

I.

1. Patient sitting quietly, and in five minutes 23 m. were collected.
2. Patient sitting and straining, and in five minutes 35 m. were collected.
3. Patient sitting quietly, and in five minutes 19 m. were collected.
4. Patient sitting and straining, and in five minutes 33 m. were collected.
5. Patient lying—lying down and not straining, 27 m. were collected.
6. Patient sitting with head overhanging in five minutes, 28 m. were collected.
7. Patient sitting with head forward, and in five minutes 15 m. were collected.

II.

1. Abdomen compressed, and in five minutes 27 m. were collected.
2. Sitting quietly, and in five minutes 14 m. were collected.

[2] The Cerebrospinal Fluid, Allbutt's System of Medicine, 1899, vii, 239.
[3] Ibid., New York, 1899.

3. Abdomen compressed, and in five minutes 24 m. were collected.
4. Sitting quietly, and in five minutes 23 m. were collected.

The experiments carried out by Hill are valueless, owing to the short space of time given to each procedure.

It is stated that the normal amount of cerebrospinal fluid present in the subarachnoid space is about 100 c.c. That this fluid is rapidly formed is shown by the enormous amount of fluid escaping from the ear of my patient. It is clear that any condition which would cause congestion of the cerebral vessels would mechanically encroach upon the subarachnoid space, thereby increasing intracranial pressure. A sudden increase of flow after straining or compressing the abdomen, and a decrease in flow when the mechanical pressure is released, is to be expected. Suffice it to say, if the straining or compression of the abdomen had been kept up for twenty to thirty minutes, Hill's observations would have been different, as will be shown later. Furthermore, Sabin has shown that the subarachnoid space is fully developed, long before the lymphatics have budded out from the subclavian and iliac veins.

Mott[4] is credited with giving the following compositions of the fluid, which he considered to be against its being a transudation from the blood or a lymphatic secretion.

1. It contains 0.02 per cent. of proteins against 7 per cent. in blood plasma and 4.5 per cent. in body lymph.
2. There is an absence of lipochroma.
3. There are no leukocytes in normal cerebrospinal fluid.
4. In enteric fever there is an absence of agglutination.
5. It has no hemolytic action on the blood corpuscles of other animals.
6. It contains no alexins.

Willis, in 1664, first mentioned the glandular appearance of what is now called the choroid plexus. Faivre, in 1853, maintained that the cuboidal cells which cover the choroid plexuses are secreting cells concerned in the formation of cerebrospinal fluid. Mott examined histologically the choroid plexus of a human subject. He reports that the sections under high power reveal tufts of vessels surrounded by a loose connective tissue covered by a single layer of cubical, spheroidal or polyhedral cells lying on a basement membrane. Around the arteries and arterioles and lying in the loose connective tissue numerous nerve fibers are seen in a form of a plexus. In the sections he also observed vacuoles in the cells, and cup-like cavities in others, as one would expect if fluid had escaped from the vacuole. He concludes, therefore, from the histological evidence that the choroid plexus is a gland with an external secretion, but with an internal destination. Being a mixed gland, he suggests

[4] The Physical and Chemical Properties of the Cerebrospinal Fluid, Oliver Sharpey's Lectures, Lancet, July 2 and 9, 1910.

that its mode of formation is in an inverse manner to those formed by epithelial invagination of glands with an excretory duct. Ependymal invagination occurs for the choroid plexus.

Kramer[5] describes the histological appearance of the choroid plexus as highly vascular projections of the pia mater into the ventricle, covered with villous-like projections about 1 to 2 mm. in diameter, under the microscope these villi are seen to be made up of a number of secondary villi about 25 mm. in diameter, which again show grape-like projections. Through the centre of the villi run comparatively thick-walled bloodvessels, giving the organ a highly vascular appearance. The connective tissue of the villi is that of the pia mater. Covering the villi of the plexus is a layer of spheroidal cells in each of which may be seen in addition to the nucleus, yellowish granules. These cells are probably the secreting cells of the organ. These cells are without ducts, pouring their secretions directly into the ventricular system of the brain.

Carl Schmidt, in 1850, advanced the chemical evidence in favor of a true secretion. Petit and Girard,[6] in 1902, demonstrated the secretory functions of the choroid plexus in different classes of vertebrates. They found that administration of substances endowed with hypersecreting action caused histological changes in the cells covering the plexus. Dixon and Halliburton have experimental proof that an intravenous injection of an extract of choroid plexus produces an increased secretion of the cerebrospinal fluid. The injections of extracts of the brain produces the same effect upon the respiration, blood-pressure and flow of the cerebrospinal fluid, as does the injection of extract of choroid plexus. So also in cases of general paralysis and brain softening, where destructive processes are actively taking place, the cerebrospinal fluid when injected, produces identical effects. They suggest, therefore, that the increase in output of fluid is due to the stimulating action of some chemical substance (harmone) in the extract on the secreting cells of the gland, and that the harmone is a product of the brain's metabolism which passes to the choroid plexus and stimulates the secreting cells of the plexus.[7]

Writers as Levy, Cushing, Obersteiner, Cavaggani, Frazier, and others likewise maintain the secretory activity of the choroid plexus as the formation of cerebrospinal fluid.

The following observations were made in the case of the patient herein reported:

[5] Fall of Pressure Produced by Choroid Extract, Jour. Amer. Med. Assoc., 1911, lvi, 265.

[6] Smith, E., The Cerebrospinal Fuild, Guy's Hosp. Gaz., London, 1911, xxv, 141.

[7] W. Mestregat, in a recent publication, expresses his belief that the cerebrospinal fluid is neither a transudation nor a secretion, but is a product of dialysis from the blood plasma.

TABLE I.

Time	Amount collected in five minutes approximate in c.c.	State of patient.	Hear rate	Analyses of cerebrospinal fluid.					Expressed as grams per 100 c.c. fluid.		
				Duration, minutes.	Actual am't, c.c.	Solids, gm.	Ash gm.	K_2O gm.	Solids.	Ash.	K_2O.
	Period I—	Control									
11.05	.73 c.c. (12 m.)	Apparently asleep	126								
11.10	1.54 c.c. (25 m.)	Apparently asleep	130								
11.15	1.23 c.c. (20 m.)	Apparently asleep	128								
				30	5.4	0.0720	0.0494	0.0008	1.35	0.91	0.015
11.20	.48 c.c. (8 m.)	Apparently asleep	130								
11.25	.49 c.c. (8 m.)	Apparently asleep	128								
11.30	.86 c.c. (14 m.)	Apparently asleep	126								
A.M.	Period II[a]										
5	.73 c.c. (12 m.)	Restless and quiet	170								
10	.37 c.c. (6 m.)	Restless and quiet	140								
15	.30 c.c. (5 m.)	Restless and quiet	163								
20	.37 c.c. (6 m.)	Restless and quiet	134								
				40	4.4	0.0676	0.0476	0.0009	1.54	1.08	0.017
25	.73 c.c. (12 m.)	Restless	170								
30	.55 c.c. (9 m.)	Restless and quiet	147								
35	.37 c.c. (6 m.)	Quiet	136								
40	.86 c.c. (14 m.)	Quiet	140								
	Period III										
45	.96 c.c. (16 m.)	Quiet	140								
50	1.50 c.c. (25 m.)	Restless and quiet	136								
55	1.38 c.c. (23 m.)	Quiet	136	25	7.2	0.0751	0.0501	0.0009	1.04	0.70	0.013
60	1.68 c.c. (28 m.)	Restless and quiet	168								
65	1.38 c.c. (23 m.)	Restless	168								
	Period IV										
70	1.20 c.c. (20 m.)	Restless	164								
75	1.14 c.c. (19 m.)	Restless	164								
				20	4.75	0.0587	0.0379	0.0006	1.24	0.80	0.013
80	1.02 c.c. (17 m.)	Restless	164								
85	1.20 c.c. (20 m.)	Restless	166								
	Period V										
P.M.	Not measured		...	90	Not measured	0.0614	0.0392	0.0007			
2.35	Period VI										
5	1.14 c.c. (19 m.)	Quiet	140								
10	1.14 c.c. (19 m.)	Quiet	138								
15	1.20 c.c. (20 m.)	Quiet and restless	145								
				30	7.0	0.0648	0.0414	0.0006	0.92	0.59	0.009
20	.96 c.c. (16 m.)	Quiet	138								
25	1.02 c.c. (17 m.)	Quiet	140								
30	1.20 c.c. (20 m.)	Quiet	140								
	Period VII										
35	1.08 c.c. (18 m.)	Apparently asleep	140								
40	.96 c.c. (16 m.)	Apparently asleep	138								
45	1.14 c.c. (19 m.)	Quiet	140								
				30	7.1	0.0930	0.0624	0.0011	1.31	0.88	0.016
50	1.14 c.c. (19 m.)	Quiet	138								
55	1.38 c.c. (23 m.)	Restless	144								
60	1.14 c.c. (19 m.)	Restless	144								
	Period VIII										
	Not measured		...	65	13	0.1530	0.1022	0.0014	2.73	1.82	0.025
P.M.	Period IX										
5	.30 c.c. (5 m.)	Restless	150								
10	.12 c.c. (2 m.)	Apparently asleep	140								
15	0.0	Apparently asleep	138								
20	0.0	Apparently asleep	136	110	6.9	0.1096	0.0632	0.010	1.59	0.92	0.014
25	0.0	Apparently asleep	136								
30	1.02 c.c. (17 m.)	Restless	140								
110	5.76 c.c. (96 m.)										
	Period X										
5	.96 c.c. (16 m.)	Apparently asleep	150								
10	1.20 c.c. (20 m.)	Apparently asleep	140								
15	1.14 c.c. (19 m.)	Apparently asleep	136								
20	1.32 c.c. (22 m.)	Apparently asleep	138								
25	2.40 c.c. (40 m.)	Apparently asleep	138	45	13.4	0.1612	0.1065	0.0015	1.20	0.80	0.011
30	1.38 c.c. (23 m.)	Restless	140								
35	1.80 c.c. (30 m.)	Apparently asleep	140								
40	1.38 c.c. (23 m.)	Apparently asleep	140								
45	1.32 c.c. (22 m.)	Restless	150								

[a] Epinephrin (1 to 1000) 5 m. injected subcutaneously. A blanching appeared at point of injection.

TABLE I—Continued.

Time	Amount collected in five minutes approximate in c.c.	State of patient.	Heart rate.	Analyses of cerebrospinal fluid.					Expressed as grams per 100 c.c. fluid.		
				Duration, minutes.	Actual am't, c.c.	Solids gm.	Ash gm.	K_2O gm.	Solids.	Ash.	K_2O.
	Period XI										
5	.80 c.c. (15 m.)	Quiet	144								
10	1.20 c.c. (20 m.)	Restless	150								
15	1.14 c.c. (19 m.)	Quiet	142								
20	1.14 c.c. (19 m.)	Quiet	140								
25	1.02 c.c. (17 m.)	Quiet	138								
30	.96 c.c. (16 m.)	Quiet	150								
35	1.14 c.c. (19 m.)	Restless	154								
40	.90 c.c. (15 m.)	Quiet	150	75	14.5	0.1607	0.0934	0.0013	1.10	0.62	0.009
45	.84 c.c. (14 m.)	Quiet	157								
50	.96 c.c. (16 m.)	Restless	170								
55	.84 c.c. (14 m.)	Restless	168								
60	.60 c.c. (10 m.)	Restless	168								
65	.60 c.c. (10 m.)	Restless	166								
		Was given water									
70	.84 c.c. (14 m.)	Quiet	150								
75	.84 c.c. (14 m.)	Apparently asleep	140								
	Period XII										
80	1.80 c.c. (30 m.)	Apparently asleep	140								
85	2.10 c.c. (35 m.)	Apparently asleep	138								
90	.84 c.c. (14 m.)	Apparently asleep	140								
95	1.20 c.c. (20 m.)	Restless	140								
100	.90 c.c. (15 m.)	Restless	144	45	12.4	0.1131	0.645	0.0008	0.91	0.52	0.006
105	.84 c.c. (14 m.)	Quiet	150								
110	1.14 c.c. (19 m.)	Restless	154								
115	1.50 c.c. (25 m.)	Quiet and restless	145								
120	1.50 c.c. (25 m.)	Quiet and restless	148								

AVERAGE OF PERIOD.

	Solids.	Ash.	K_2O
I	1.35	0.91	0.015
II to X (except V)	1.38	0.91	0.014
XI and XII	1.02	0.59	0.008

PERCENTAGE OF ASH IN TERMS OF TOTAL SOLIDS.

I	68.6	V	63.9	IX	57.8
II	71.9	VI	63.9	X	66.1
III	66.7	VII	67.3	XI	58.1
IV	64.6	VIII	66.8	XII	57.0

AVERAGE.

I	68.6	II to X (inc. V)	65.3	XI to XII	57.7

The table summarizes the amount of fluid excreted in five consecutive minutes, the state of the patient, whether quiet, restless or apparently asleep and the heart rate. (The heart rate was taken twice in each five minute period, with a stethoscope, and the average recorded.) The fluid was collected in sterile glass test-tubes, labeled periods I, II, III, IV, V, VI, VII, VIII, IX, X, XI, XII. The tubes were given to Dr. Charles H. Frazier, who in turn secured the valuable service of Dr. A. E. Taylor, professor of physiological chemistry in the University of Pennsylvania, for chemical analysis.

March 20. Epinephrin (1 to 1000) 5 m. injected subcutaneously into the arm. Eight hours and forty minutes later atropin sulphate, gr. $\frac{1}{250}$, was injected hypodermically. Experiment begun at 11 A.M.

TABLE II.

At 3.35 water, ℥iv, given by mouth, and twenty-five minutes later atropin sulphate, gr. $\frac{1}{200}$, hypodermically.

Time.	Approximate amount in c.c.	State of patient.	Heart rate.
2:35			
5	2.70 c.c. (45 m.)	Quiet	134
10	2.70 c.c. (45 m.)	Quiet	130
15	2.40 c.c. (40 m.)	Quiet	134
20	2.70 c.c. (45 m.)	Quiet	132
3:00	Atropin, 0.05 gr. hypodermically.		
5	2.40 c.c. (40 m.)	Restless	140
10	1.50 c.c. (25 m.)	Restless	145
15	1.50 c.c. (25 m.)	Quiet	138
20	1.50 c.c. (25 m.)	Quiet	136
25	.96 c.c. (16 m.)	Quiet and restless	138
30	1.14 c.c. (19 m.)	Quiet and restless	136
35	1.32 c.c. (22 m.)	Quiet and restless	138
40	1.08 c.c. (18 m.)	Apparently asleep	138
45	1.26 c.c. (21 m.)	Apparently asleep	140
50	1.14 c.c. (19 m.)	Apparently asleep	138
55	.90 c.c. (15 m.)	Apparently asleep	140
60	.90 c.c. (15 m.)	Apparently asleep	138
65	.96 c.c. (16 m.)	Apparently asleep	144
70	.60 c.c. (10 m.)	Apparently asleep	140
75	.90 c.c. (15 m.)	Apparently asleep and restless	144
80	1.02 c.c. (17 m.)	Apparently asleep	138
85	.90 c.c. (15 m.)	Apparently asleep	138
Milk is given.			
90	.66 c.c. (11 m.)	Restless	145
95	1.38 c.c. (23 m.)	Restless	146
100	1.32 c.c. (22 m.)	Restless	144
105	——	Exceedingly restless	...
110	.96 c.c. (16 m.)	Restless	146
115	.96 c.c. (16 m.)	Restless	144
120	.90 c.c. (15 m.)	Restless	150

TABLE III.—TO SHOW THE INFLUENCE OF SLEEP, QUIET, AND RESTLESSNESS UPON THE SECRETION OF CEREBROSPINAL FLUID, MARCH 22.

Time.	Approximate amount collected in 5 minutes in c.c.	State of patient.	Heart rate.
11:00	.30 c.c. (5 m.)	Quiet	134
5	1.08 c.c. (18 m.)	Quiet and restless	134
10	1.08 c.c. (18 m.)	Quiet	135
15	.60 c.c. (10 m.)	Restless and Quiet	145
20	.90 c.c. (15 m.)	Quiet	134
25	.90 c.c. (15 m.)	Quiet	140
30	.96 c.c. (16 m.)	Quiet	140
35	1.14 c.c. (19 m.)	Quiet	138
40	1.38 c.c. (23 m.)	Quiet and restless	144
45	1.14 c.c. (19 m.)	Quiet and restless	142
50	1.08 c.c. (18 m.)	Quiet	134
55	1.50 c.c. (25 m.)	Quiet	136
60	1.14 c.c. (19 m.)	Quiet and restless	140
65	1.08 c.c. (18 m.)	Quiet and restless	144
	COLLECTED THE FOLLOWING DAY, MARCH 23.		
11:00 A.M.			
5	.90 c.c. (15 m.)	Quiet and restless	140
10	.84 c.c. (14 m.)	Quiet and restless	138
15	1.02 c.c. (17 m.)	Quiet and restless	140
20	2.28 c.c. (38 m.)	Quiet	138
25	1.38 c.c. (23 m.)	Quiet and restless	142
30	.90 c.c. (15 m.)	Restless	150
35	.96 c.c. (16 m.)	Restless	144

A Summary of the Effect of Atropin on Cerebrospinal Flow.—Table I. The normal secretion during one hour amounted to 17.7 c.c., average heart rate was equal to 139 beats per minute. After the injection of atropin, gr. $\frac{1}{250}$ hypodermically, the amount of secretion during one hour amounted to 11.8 c.c., a decrease of 5.9 c.c. in one hour. Average heart beat 153 per minute, an increase of 14 beats to the minute.

Table II. The normal secretion for twenty minutes amounted to 10.8 c.c., or at the rate of one hour, 32.3 c.c.; average heart beat per minute 132. After injection of atropin, gr. $\frac{1}{200}$ hypodermically, the amount secreted in the first twenty minutes amounted to 7.1 c.c. a decrease of 3.7 c.c. in twenty minutes. Average heart rate 138 per minute, an increase of 6 heart beats. The amount secreted in one hour was 16.1 c.c. a decrease of 16 c.c. for one hour. Average heart beat 141 per minute, an increase of 9 heart beats per minute. The amount secreted the following thirty minutes at the rate of one hour was 14.1 c.c. The chemical analysis of Table I shows a diminished solid, ash and potassium[9] content with an increased volume of fluid per time unit after injection of atropin. From the above observations it would undoubtedly follow that atropin exerts a partial inhibitory influence upon the secretion of cerebrospinal fluid; that is to say, atropin depresses the nervous stimuli of certain secretory cells of the choroid plexus in the same manner as it does other glands of the body dependent upon nervous stimuli for their secretion. Capelleti has shown that on dogs, atropin and hyoscyamin diminished the flow of cerebrospinal fluid, while pilocarpin increased it. Yoshimura states that atropin produces microscopical changes which are a manifestation of the inhibitory influence brought to bear on the secretory activity of the cells. Dixon and Halliburton[10] have found that after the administration of atropin, subsequent injection of choroid extract produces an increase of cerebrospinal flow.

The decrease in secretion of cerebrospinal fluid can be explained by one of two ways: (1) By granting that there is only one type of secretory nerves in the choroid plexus, and that the activity of the nerve endings depends entirely upon the presence of a chemical substance or harmone, and that the harmone is produced by the choroid cells themselves, atropin[11] would decrease the flow then, by depressing the cells which give rise to the formation of the harmone. The increase in flow following the injection of choroid extract, after the animal has been atropinized would be due to the mechanical replacing of a substance necessary for the stimulation

[9] The potassium was determined by the volumetric method of Drushel (cobaltinitrite method), and was not done in duplicate, as the amount of fluid was too small.

[10] Jour. of Physiol., 1913, xlvii.

[11] These secretions dependent upon nervous stimuli are depressed; those dependent upon chemical stimuli are unaffected by the action of atropin.

of the cells to secretion. It is not likely that this gland produces its own harmone. We know of no other gland in the body where such a mechanism occurs. It has been shown further that the extract of the brain and cerebrospinal fluid in general paralysis contains a harmone similar to that found in the choroid plexus. (2) It is more plausible to speculate that the gland is supplied with two sets of secretory nerves, namely: those dependent upon nervous stimuli for their action, the remaining ones dependent on chemical stimuli for their activity. The former would explain the diminution in flow after the injection of atropin. The latter would explain the increase after the injection of choroid or brain extract. Dixon and Halliburton suggest that the chemical stimuli or harmone are some part of the product of the brain's metabolism.

Summary of the Effect of Epinephrin on Flow of Cerebrospinal Flow. Table I. The normal secretion for thirty minutes amounted to 5.4 c.c. or in terms of sixty minutes 10.8 c.c. Average heart rate 128 beats per minute. After the injection of adrenalin (1 to 1000) ℥v subcutaneously, the amount secreted in the first thirty minutes amounted to 3.1 c.c., or in terms of one hour, 6.1 c.c., a decrease of 2.3 c.c. in thirty minutes, or in terms of sixty minutes a decrease of 4.7 c.c. Average heart rate for thirty-five minutes after injection of adrenalin was 150.

The following fifty minutes the secretion at the rate of an hour was 15.2 c.c. Three hours after the injection, the blanching upon the arm becoming smaller, the secretion amounted to 14 c.c. per hour. Five hours after the injection the secretion amounted to 13 c.c. per hour. Six hours later the blanching on the arm had entirely disappeared. The secretion gradually diminished and ceased entirely for fifteen minutes, the child apparently being asleep. The child became restless and the secretion began to flow again. The first five minutes amounted to 1.06 c.c. The collection for the following eighty minutes was 5.9 c.c. Seven hours after the injection the secretion collected in sixty minutes amounted to 17.7 c.c.

The chemical analysis of the fluid following the injection of epinephrin shows such marked variations that it would be stretching a point to attempt an interpretation.

We notice, then, that after the injection of epinephrin the secretion is diminished a little more than one-half in the first thirty minutes. Frazier has likewise reported a marked diminution in his experiments on dogs. What is the explanation? Does epinephrin constrict the cerebral vessels, and by decreasing the blood supply to the choroid plexus diminish the cerebrospinal flow?

The increase in pressure in the circle of Willis after the injection of epinephrin, as is found by Biedl and Reiner, and the decrease in flow from the external jugular vein, reported by Pick, point to a local constriction in the cerebral arterials. In experiments made

upon an isolated brain (in the skull) perfused with an artificial circulation, Wiggers[12] states that the addition of epinephrin causes a diminution in outflow from the organ. He believes the drug constricts the cerebral vessels in the same manner as it does vessels of other organs, and therefore suggests the existence of cerebral vasoconstriction nerves. On the other hand, Bayliss and Hill experimentally could discover no constricting effect of epinephrin on the cerebral vessels. Gerhardt concludes that nothing more than a passive dilatation occurs within the cranium. Dixon and Halliburton, as a result of their experiments on dogs, state that they have never observed constriction of the cerebral vessels from the use of epinephrin, and they challenge the technique as carried out by Wiggers.

Guillard, Huber, and Hunter have demonstrated that the vessels of the brain are provided with perivascular nerve plexuses. But writers as Roy and Gherrington, Hill Wagner[13] and others from their experimental studies conclude that the cerebral vessels do not possess vasomotor nerves. Masso,[14] as quoted by Howell, has shown by observation upon men with trephine holes in the skull that the constriction of the limbs is always accompanied by dilatation of cerebral vessels. Cushing[15] states that only those vessels of the body that receive nerve fibers from the thoracicolumbar cord are constricted by epinephrin. The blood is, therefore, diverted from the organs supplied by the thoracicolumbar segment, and as a result the cerebral vessels become passively dilated. Suffice it to say, experimental evidence points to the non-constricting action of epinephrine on the cerebral vessels. Further, Frazier[16] has shown experimentally that ligation of both carotids in dogs, thereby decreasing the blood-supply to the choroid plexus has no retarding influence on the rate of the secretion of cerebrospinal fluid. He has also demonstrated that the injection of saline extracts of certain organs, especially of the liver, kidney, spleen and pancreas, caused a fall in blood-pressure, and at the same time a marked increase in flow of cerebrospinal fluid. Likewise amyl nitrate produced an increase in flow of the fluid. On the other hand, he has shown that the injection of epinephrin caused a rise of blood-pressure, and coincident with this a marked decrease in flow of cerebrospinal fluid. That is to say the general rise in blood-pressure accompanied by an increased flow of blood through the brain, and increased intracranial pressure, is followed by a diminution of cerebrospinal secretion, and the fall in blood-pressure which is accompanied by a decrease in flow of blood through the brain and decreased intra-

[12] Am. Jour. Physiol., 1905, xiv, p. 452.
[13] Howell, W. H., Text-book of Physiology, Philadelphia, 1907, p. 580.
[14] Ibid., p. 579.
[15] Text-book of Pharmacology and Therapeutics, Philadelphia, 1910, p. 334.
[16] The Cerebrospinal Fluid as a Problem in Intracranial Surgery, Jour. Amer. Med. Assoc., 1914, lxiii, 287.

of the cells to secretion. It is not likely that this gland produces its own harmone. We know of no other gland in the body where such a mechanism occurs. It has been shown further that the extract of the brain and cerebrospinal fluid in general paralysis contains a harmone similar to that found in the choroid plexus. (2) It is more plausible to speculate that the gland is supplied with two sets of secretory nerves, namely: those dependent upon nervous stimuli for their action, the remaining ones dependent on chemical stimuli for their activity. The former would explain the diminution in flow after the injection of atropin. The latter would explain the increase after the injection of choroid or brain extract. Dixon and Halliburton suggest that the chemical stimuli or harmone are some part of the product of the brain's metabolism.

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upon ate for the diagnosis and treatment of all the surgical ills to
cerebellopontile human nature is heir. We are informed, moreover,
a chair has been endowed and named Allen, between Drury-
constructed vertical streets on the south to the Gilmore Avenue
of other general hospitals, is, of course, the advertisement
vasoconstrictor nerves. Yet the hospital that Dr. Murphy and his
experimentally could discover no constricting effect of epinephrin
on the cerebral vessels. Of the volumes, there is included
than a passing allusion to a work of Dr. Murphy, seated in his boudoir,
Halliburton, he account of their experiments of his countenance skilfully
have served the mind constriction of the cerebral vessels from the
use of epinephrin, and they challenge the technique as carried out
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"Upon what meat doth this our Murphy feed,
That he is grown so great? Age, thou art sham'd!
But he is armed with more than with one mark!
[illegible]"

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decreasing the blood-supply to parts of which is handsomely acknowl-
influence on the practice the present edition. Though this preface
also demonstrates considerable revision has been required, and that
organs is plainer, have been entirely rewritten, it is apparent even
a full and cursory survey of the volumes that a more extensive revision
flow of rewriting would have been required to make them represent
contemporary knowledge in all the subjects included.

Though Moynihan employs, and describes with adequate illus-
trations, Crile's methods of "anoci-association technique" in making
the abdominal incision (which is an evidence of modernity), he yet
persists in employing irrigation in acute peritonitis, and advises
making in such cases from three to five counter-incisions for pur-
poses of drainage. He also recommends that a glass tube be run
up the lumen of the bowels to secure their evacuation, during
operations for acute peritonitis; this, he adds, should be "considered
an almost routine practice."

There is nothing about "Lane's kink," nor about "cæcum mobile,"
and not enough about visceroptosis. The statistics of the operation
for intestinal perforation in typhoid fever have not been brought

cranial pressure results in an increased secretion of cerebrospinal fluid.

It would appear that the cerebrospinal fluid which fills the space of the cranial cavity not occupied by vessels and nerves adjusts the mechanism of the circulation of the brain tissue by equalizing pressure. So nature has adjusted, so to speak, through its nervous mechanism, the secretion of the choroid plexus in such a way, that the activities of the cells are diminished when there is a rise in blood-pressure (increased intracranial pressure) and an increase in the activities occurs when the blood-pressure falls (decreased intracranial pressure). There is then a certain inverse relationship between the blood-pressure (intracranial pressure) on the one hand and the secretory activities of the choroid plexus on the other, and this relationship has the characteristics of a purposeful adaptation. Therefore, the diminution of flow which occurs after the injection of epinephrin is to be explained by the inverse relationship between blood-pressure and the secretory activity of the choroid plexus.

The fact that a marked increase of secretion occurred forty minutes after the injection of epinephrin is to be explained on the ground that the action of the drug had been spent[17] by this time and as a result the blood-pressure fell with a corresponding incresae in flow of cerebrospinal fluid. I was particularly attracted while making my observations and perplexed at the time to find, when collecting my controls, or when urotropin was given, that the secretion invariably decreased when the child was restless, and increased when asleep. At times the patient would be in a violent anger, striking as I would attempt to collect the fluid, and if the hands were held, would toss, scream, and contract violently every muscle. During the entire procedure we were amazed to find the secretion markedly decreased. At other times, after the child had been asleep for some time, restlessness would cause a momentary increase in flow, which is to be explained upon a mechanical basis. However, if the restlessness existed any length of time the momentary increase would be followed by a decrease in flow for the entire time of restlessness. (See TABLE III). This likewise carries out the inverse relationship between the blood-pressure which rises during restlessness, and falls during quietude and sleep, and the secretory activity of the choroid plexus, and further substantiates the purposeful adaptation theory. In pathological cases, however, this does not hold good. Here we are dealing with a degenerative process which is taking place in the brain tissue, causing an increase in brain metabolism. Thus there is added to the blood stream a superabundance of harmones, which in turn stimulates those cells

[17] The action of epinephrin when injected intravenously is of short duration. When injected subcutaneously it causes a blanching at the point of injection and in large doses the blanching acts as a reservoir, so to speak, for renewed supply.

of the gland dependent upon a chemical stimulus for their activity to hyper-secretion.

We also noticed that there was a marked increase in secretion ten to fifteen minutes after the intake of water; and a very slight change, if any, after the intake of milk. Throughout the entire observations, the pulse rate bore absolutely no relationship to the amount of secretion.

The child was given, on different occasions, large doses of urotropin by mouth, and the cerebrospinal fluid collected in sterile glass tubes at five-minutes intervals for several hours after the intake of the drug. We hope within the near future to publish the results of the appearance and disappearance of urotropin in cerebrospinal fluid, as is found in the case of the patient herein reported.

We wish to express our great indebtedness to Dr. Louis Mutschler, under whose service the child was treated, for kindly permitting us to publish full observations of the case.

REVIEWS

DISEASES OF THE BRONCHI, LUNGS, AND PLEURA. By FREDERICK T. LORD, M.D., Visiting Physician, Massachusetts General Hospital, etc.; Instructor in Clinical Medicine, Harvard Medical School. Pp. 605; 93 engravings and 3 colored plates. Philadelphia and New York: Lea & Febiger, 1915.

THE book itself is an exhaustive and altogether satisfactory grouping of the diseases of the respiratory tract with the exception of tuberculosis, which, on account of its length, is necessarily excluded. It is divided into three sections, as indicated by the title, and, as would be expected, more than half of the volume is devoted to diseases of the lungs. The chapter on bronchial asthma devotes considerable space to the theories of its causation, but does not attempt to decide the matter. He suggests that whether the immediate cause lies in the bronchial mucous membrane or in the bronchial muscles or both, some internal or external underlying factor must be assumed to exist. The infectiousness of the condition of acute tracheobronchitis is regarded as settled and the influenza bacillus receives most of the blame. Chronic bronchitis, he rightly argues, is usually to be regarded as merely a symptom of some more important basal process.

The chapter on lobar pneumonia is the longest in the book and deals very completely with the subject. The bacteriology and the questions of animal experimentation and immunity receive considerable space, and the symptoms, physical signs, and treatment are given ample attention. Very little mention, however, is made of the out-of-door treatment, of which the author apparently does not approve.

He states that hemoptysis may occur more or less frequently in fifteen different conditions, but tuberculosis must be considered guilty until proved innocent. He regards pulmonary syphilis as a rare condition and hard to diagnose. Other clinicians, however, claim to have observed it more frequently.

He believes that tuberculosis is also the cause of the majority of the cases of acute serofibrinous pleuritis. He does not place himself among the extreme radicals who believe there is no exception to this rule, but he argues that while all cases cannot be so classed, it is best for purposes of treatment to assume it in every case unless there is good reason to believe otherwise. Thoracentesis is given

a detailed description, including the indications, the technique, and the difficulties likely to be encountered.

A number of the less commonly met diseases of the lungs, such as actinomycosis, streptothricosis, blastomycosis, and aspergillosis, are presented along with a chapter on animal parasites and tumors.

It can safely be recommended as a reliable and handy reference work, in the preparation of which the author has drawn largely on his own researches and clinical experience and on clinical and pathological data which has accumulated in the Massachusetts General Hospital. S. J. R.

A Text-book of Diseases of the Nose and Throat. By D. Braden Kyle, A.M., M.D., Professor of Laryngology and Rhinology, Jefferson Medical College, Philadelphia. Fifth edition, thoroughly revised and enlarged. Octavo, 856 pages; 272 illustrations, 27 in colors. Philadelphia and London: W. B. Saunders Company, 1914.

The fifth edition of this already well-known work has been brought up to date in all essentials. The following new articles have been added: vaccine therapy; lactic bacteriotherapy in atrophic rhinitis; salvarsan in the treatment of syphilis of the upper respiratory tract; sphenopalatine ganglia neuralgia; negative air pressure in accessory sinus diseases; chronic hyperplastic ethmoiditis; congenital insufficiency of the palate. The chapter on tonsils has been revised, with the addition of the Sluder operation and technique brought up to date.

In many of the chapters additional information has been incorporated; such as the ocular symptoms in diseases of the nasal cavities; correction of septal deformities (various methods); thymic asthma, and many other subjects. A number of new illustrations have been added, and many of the older ones have been replaced by new.

As in former editions the striking feature of the book is the descriptive pathology brought out in connection with each subject, Dr. Kyle for many years being an authority on the pathology of the upper respiratory tract.

Though at times there is some repetition in the text, it is apparent that the author is desirous to make each subject concise and complete, and to save the reader the unnecessary obligation to refer elsewhere.

Dr. Kyle's book is as much for the student and general practitioner as for the specialist; the subject matter going into the many elementary details may be easily found by reference to the very voluminous and well-arranged index, which covers fifty-one pages. B. D. P.

OBSTETRICAL NURSING. A MANUAL FOR NURSES AND STUDENTS AND PRACTITIONERS OF MEDICINE. BY CHARLES SUMNER BACON, PH.B., M.D., Professor of Obstetrics, University of Illinois, and Chicago Polyclinic; Medical Director, Chicago Lying-in Hospital, etc. Pp. 355; 123 illustrations. Philadelphia and New York: Lea & Febiger, 1915.

THE book opens with a short introductory chapter on the ethics concerned in obstetrical nursing. The second chapter deals with anatomy, physiology, and embryology in such a manner as to simplify to the nurse their relation to a study of pregnancy and labor. Pregnancy is considered in the second chapter in both its normal and abnormal aspects. The sections on the management of pregnancy and the pathological changes of pregnancy may well be commended to the careful study of the prenatal visiting nurse.

A full third of the book is devoted to labor. Thorough instructions are given for the guidance of the nurse often in sole charge of the patient for the greater part of this period. The chapter is replete with practical expedients. The object and general character of obstetrical operations are included. The care of the puerperal woman is discussed at length in Chapter V. The care of the infant forms the subject of the concluding chapter which gives an excellent outline for the care of the premature infant.

The principles governing this particular and important department of nursing are admirably presented, and the book may be heartily recommended as an aid in the practice of obstetrical nursing.

P. F. W.

THE CLINICS OF JOHN B. MURPHY, M.D., at Mercy Hospital, Chicago. Vol. III, No. 5 and No. 6, October and December, 1914. Pp. 190 and 175; 113 illustrations. Philadelphia and London: W. B. Saunders Company, 1914.

THESE numbers conclude the third volume of Murphy's *Clinics*. Each contains one or more "Clinical Talks on Diagnosis," besides the usual variety of case reports, with Dr. Murphy's incisive, caustic, but withal entertaining and instructive comments. In addition, the last number contains a splendid advertisement of Dr. Murphy's new offices, showing a ground plan of the arrangement of the apartments assigned to himself and to various members of his staff, and numerous photographs of interiors and exteriors, bringing forcibly to the attention of the reader what great facilities are

afforded for the diagnosis and treatment of all the surgical ills to which poor human nature is heir. We are informed, moreover, that "The building is situated on Calumet Avenue, between Twenty-fifth and Twenty-sixth Streets, next door to the Calumet Avenue entrance to Mercy Hospital. It is, of course," the advertisement continues to read, "at Mercy Hospital that Dr. Murphy and his staff do all their work."

To enhance the interest of the volume, there is included an admirable full-length portrait of Dr. Murphy, seated in his boudoir, and with the "counterfeit presentment" of his countenance skilfully reflected in a mirror.

"Upon what meat doth this our Murphy feed,
That he is grown so great? Age, thou art sham'd!
Chicago has lost the breed of noble bloods!
When went there by an age, since the great fire,
But it was fam'd with more than with one man?"

παντὰ κόνις καὶ παντὰ γέλως καὶ παντὰ τὸ μηδέν.

A. P. C. A.

ABDOMINAL OPERATIONS. By SIR BERKELEY MOYNIHAN, M.S. (London), F.R.C.S., Leeds, England. Third edition; two volumes. Pp. 488 and 492; 371 illustrations. Philadelphia and London: W. B. Saunders Company, 1914.

MOYNIHAN'S *Abdominal Operations* well deserves the popular esteem it has won with the profession in America, the author's indebtedness to many members of which is handsomely acknowledged in the preface to the newest edition. Though this preface also tells us that a considerable revision has been required, and that certain chapters have been entirely rewritten, it is apparent even from a cursory survey of the volumes that a more extensive revision and rewriting would have been required to make them represent contemporary knowledge in all the subjects included.

Though Moynihan employs, and describes with adequate illustrations, Crile's methods of "anoci-association technique" in making the abdominal incision (which is an evidence of modernity), he yet persists in employing irrigation in acute peritonitis, and advises making in such cases from three to five counter-incisions for purposes of drainage. He also recommends that a glass tube be run up the lumen of the bowels to secure their evacuation, during operations for acute peritonitis; this, he adds, should be "considered an almost routine practice."

There is nothing about "Lane's kink," nor about "cecum mobile," and not enough about visceroptosis. The statistics of the operation for intestinal perforation in typhoid fever have not been brought

up to date; indeed, it does not appear that any changes in this chapter have been made since the publication of the first edition of the work.

In performing gastrectomy, Moynihan first ligates the pyloric artery and severs the pylorus; then turns the stomach far to the patient's left, divides the coronary artery, and completes the gastro-enterostomy before detaching the diseased portion of the stomach. He still credits E. J. Senn with Stamm's method of gastrostomy. *Capitonnage* is confused with marsupialization of hydatid cysts of the liver.

A frequent error is repeated in describing Kocher's gall-bladder incision: It is described and illustrated not as either described or illustrated by Kocher himself, but as lying chiefly to the outside of the semilunar line, instead of almost entirely over the rectus muscle. The fact that Kehr has abandoned (since 1912) the lower limb of his "Wellenschnitt" is ignored, and Czerny's incision is not mentioned, though incisions recently described by Don and by Perthes, and which are virtually modifications of Czerny's, are noted. Nor is Sprengel's transverse incision mentioned; it appears to be gaining in favor in many quarters.

Moynihan strongly favors cholecystectomy. He writes: "During the last eight years I have inclined more and more to the performance of cholecystectomy, and after some hesitation and some trepidation, which experience has removed, I am strongly disposed to advocate the frequent, though certainly not the invariable, adoption of this operation in preference to cholecystotomy in view of the character of the cases that submit themselves to surgical treatment."

Though the beauty of the illustrations and the charming simplicity of the description of the steps of the operations remain, yet we are forced to acknowledge, and we do it with sincere regret, that the present edition is less representative of contemporary abdominal surgery than were either of the editions which have preceded it.

A. P. C. A.

On Dreams. By Prof. Dr. Sigm. Freud. English Translation by M. D. Eder from the second edition. Pp. 110. New York: Rebman Company, 1914.

This is a popular edition of Freud's work on dreams, and is an English translation of a German work by M. D. Eder. The introduction is by the well-known English alienist W. Leslie McKinsey. Dr. McKinsey, like other English neurologists, is gradually beginning to appreciate the psychological value of some of Freud's work. It is questionable whether in this small volume of 110 pages one can

get more than an impression of the subject matter, but perhaps this is all that is intended. If one is interested more seriously the larger work, of which there is an English translation, should be consulted.

T. H. W.

ORTHOPÄDISCHE CHIRURGIE. By DR. GUST. ALBERT WOLLENBERG. Pp. 258; 147 illustrations. Klinkhardt: Leipsic.

THIS hand-book, which is about to be discussed, is in German, which fact diminishes largely its value in the hands of the average American orthopedist. The order of this book is practically the same as that which is followed by most orthopedists. There is nothing specially original in the illustrations and they are of no special value. The methods advocated herein are the usual methods which are found in the practice of the average orthopedist. There is a moderate claim to originality in certain of the methods advised, but close comparison with the work of other men shows that the underlying principles of the methods in question are a common commodity. In the treatment of scoliosis there is a rather general collection of the various methods used by the leading orthopedists in the treatment of the various stages of this affection. It omits, however, an intelligent discussion of the latest methods employed for the correction of spinal curvature and certain other orthopedic procedures. To the person who reads German fluently this book would be valuable from the point of view of interest in the work of the author, but as a scientific addition to the orthopedist's library the reviewer can lay no special stress upon this work.

W. J. M.

THE EVOLUTION OF ANATOMY. By J. EWING MEARS, M.D., LL.D. Pp. 26; 6 illustrations. Philadelphia: Wm. J. Dornan, 1914.

THIS book of about seven thousand words contains briefly the history of evolution in the study of anatomy. The average student of anatomy as he enters this field of science has no conception of the hardships through which the earlier investigators passed unless he has acquainted himself with some of the facts which this little volume contains. The names of investigators from Hippocrates down to the present time are given, with a brief *resume* of their achievements. The different epochs in the development of knowledge of human anatomy are clearly defined, and the work accomplished during this

time is presented in an attractive manner. The value of this work is especially historical, and the facts which is contains should be a ready asset in the knowledge of a present-day anatomist.

W. J. M.

THE INTERVERTEBRAL FORAMEN. By HAROLD SWANBERG, A.M., Ph.D., M.D. Pp. 101; 16 plates. Chicago Scientific Press, 1914.

THIS book is given somewhat in a tabular form. The anatomical relationships under normal conditions are accurately described and the book bears evidence of careful research. It is a well-known fact that a large group of symptoms originating in the spinal structures are due to mechanical defects in the complex structure of this part of the human anatomy. How much slight defects in this mechanical arrangement may be the cause of vasomotor and nerve disturbances is not absolutely known. Iuvestigations of Swanberg emphasize the fact that slight changes in relationships in the spinal structures may give rise to varied symptoms. The work here presented is highly commendable, and bears evidence of a thorough and careful investigation. To persons interested in nervous diseases and also in mechanical disturbances of the spine this book should be of unusual interest and value.

W. J. M.

NERVOUS AND MENTAL DISEASES. By JOSEPH DARWIN NAGEL, Consulting Physician to the French Hospital of New York; Member of the New York Academy of Medicine. Second edition. Pp. 293; 51 illustrations. Philadelphia and New York: Lea & Febiger, 1914.

THIS is the second edition of this manual. The reviewer who has taught neurology for over ten years in medical schools, has come to the conclusion that manuals and primers of any specialty are of necessity of limited value. How can a large subject like nervous and mental diseases be presented in 280 short pages in which about one-third the space is covered by diagrams? For example, the subject of cerebral localization, to which the reviewer in his third-year class gives ten hours, is covered in about six pages, most of these being made up of diagrams, and in one diagram of "the lateral aspect of the left hemicerebrum, showing the cortical centres," the motor centres are placed on either side of the central fissure. However, considered as a manual, the book is not without merit, and as a supplementary text-book will prove helpful to students.

T. H. W.

MEDICAL LABORATORY METHODS AND TESTS. By HERBERT FRENCH, M.A., M.D. (Oxon.), F.R.C.R. (Lond.). Third edition. Pp. 202; 88 illustrations. Chicago: Chicago Medical Book Co.

THE third edition of this excellent handbook, introducing new methods and tests and modifying old ones, will be welcomed by those who have used it in the past and will prove a valuable addition to the armamentarium of the general practitioner or student who is, as yet, unfamiliar with it.

In addition to the more or less limited number of tests, applicable in the past as routine measures, in the work of the general practitioner this little work has made others, such as the quantitative estimation of urea, uric acid, chlorides, sulphates and ammonia in the urine, tests for occult blood in the stools and reactions for the more common poisons and drugs, available at but little outlay of time and money. A. A. H.

URGENT SURGERY. By FELIX LEJARS, Professeur Agrégé a la Faculté de Medicine de Paris; Cherurgien de l'Hospital Saint Antoine; Membre de la Saciete Cherurgie. Vol. I, seventh edition. Pp. 614; 1086 illustrations and 20 plates. New York: Wm. Wood & Co., 1914.

THIS volume covers Head, Neck, Chest, Spine, and Aldomen. It is the third translation into English of the seventh French edition. In this last edition the work has been enlarged, revised, and remodeled. Chapters have been added on acute dilatation of the stomach, acute pancreatitis, obstruction of the mesenteric vessels, sigmoiditis, perisigmoiditis, and dislocations of the pelvis, and 92 more figures.

The author has taken up the matter of urgent surgery from the practical standpoint. There exists no theoretical discussions, no complex descriptions of untried methods or tiresome bibliography. In the introduction is outlined preparations and equipment, anesthesia and minor surgery in detail. Thereafter the book is arranged in chapters according to the region affected thus enabling the reader to refer to his subject readily without even the help of the index.

Throughout the work the author has made numerous fine print footnotes on subjects and facts that although not of primary importance, nevertheless, are well worth giving restricted space. The text is well presented, clear, concise, and reads easily and entertainingly, and frequently shows its French origin although translated into English.

The book is a good one and should be in every active practitioner's library. E. L. E.

MANUAL OF SURGERY. By ROSE AND CARLESS. Revised by ALBERT CARLESS; M.B., M.S., (Lond.) F.R.C.S. Professor of Surgery in, and Surgeon to, King's College Hospital; Consulting Surgeon to King Edward's Memorial Hospital, etc. Ninth edition. Pp. 1408; 609 illustrations and colored plates. London: Wm. Wood & Co., 1914.

THIS manual endeavors to meet and judging by the number of editions has met the present day needs of the body of its readers. It was written for students and general practitioners. It is in no sense a system on the subject, but does cover fully all the points that a student should know and further fulfils to a great extent the role of a working book for the practitioner. Facts are presented in a concise and clear manner. Theories and bibliographical references are relegated to a minor position. Subjects which are rarely met with or which bear only a slight relation to surgery are fine typed and presented in compact form. The special branches of surgery: eye, ear, etc., are touched upon and considered as fully as may be needful to the general worker. In fact, for its size the book furnishes a wonderful amount of detailed consideration of its many subjects.

This, the ninth and latest edition has added many new illustrations and a few colored plates, and a new chapter on heat, light, electricity, anoci-association, etc., without adding additional pages and hence bulk to the book. E. L. E.

ELEMENTARY BIOLOGY, ANIMAL AND HUMAN. By JAMES EDWARD PEABODY, Head of the Department of Biology, Morris High School, Bronx, and ARTHUR ELLSWORTH HUNT, Head of the Department of Biology, Manual Training High School, Brooklyn, New York City. Pp. 212; 228 illustrations. New York: MacMillan & Co.

THIS is an elementary text-book embracing those subjects in general biology which lead up to human biology. Insects, fishes, protozoa and bacteria are emphasized in their economic and hygienic relations for obvious reasons. The effect of the book is to give the principles upon which the human body is constructed and upon the physiology which keeps it healthy; in other words the basic principles of hygiene. The book further aims to interest the young student in natural history and to teach him the conservation of animals. There are outlines of study, laboratory exercises and a bibliography. H. F.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

CHIEF OF THE DEPARTMENT OF INTERNAL MEDICINE, CLIFTON SPRINGS SANATORIUM AND HOSPITAL, CLIFTON SPRINGS, NEW YORK.

The Specificity of Cholesterin Antigens in the Wassermann Reaction.—WALKER (*Arch. Int. Med.*, 1914, xiv, 563) bases this report upon the examination of 1000 Wassermann reactions performed on the blood and spinal fluids of 800 different individuals. As a knowledge of the technique used is necessary for the intelligent interpretation of results, Walker describes his method in some detail, and special emphasis is put upon the antigen used, an alcoholic extract of human heart reinforced with 0.4 per cent. cholesterin. This antigen has the advantage of being easily made from any human heart; its antigenic properties are quite constant; and it is sensitive, but not in a non-specific way with the luetic sera from patients in the late stages of the disease. The antigen must simply be accurately controlled to eliminate the disadvantages which have been advanced against it. In the series, 667 gave a negative reaction, and in none of these was lues suspected. Of the 110 who gave complete fixation there was no evidence of a false reaction; 24 sera showed incomplete hemolysis, and in all of these there was evidence of lues which had been favorably modified by treatment. Even when the antigen was used 1 to 6, a dilution near the anticomplementary dose, no false complete inhibitions were noted in 400 instances. A second part of the article deals with Walker's titration methods; the amount of serum necessary to give fixation varies in different people, even in the same stage of the disease, but if the amount of serum necessary is determined, then it can be shown that the amount of antigen necessary is a constant in different individuals in the same stage of the disease. By this method Walker claims to be able to tell an early from a late rash, and to distinguish an aneurysm from a slight aortic

dilatation. Using the least amount of serum necessary to give fixation and then determining the minimal amount of antigen required to bind with the serum, he was able to show by increasing the amount of serum that it became possible to use a proportionately smaller amount of antigen to give fixation. By these and other experiments it became clear that cholesterin is the specific agent which, in the presence of complement, binds with a syphilitic serum.

The Normal Diastase-content of the Urine.—Brown and Smith (*Johns Hopkins Hosp. Bull.*, 1914, xxv, 213) have studied the diastase content of the urine, with a view to finding out a normal value, hoping that variations might prove of value in the diagnosis of pancreatin disease, and that the test might further serve as a reliable test of renal function. The twenty-four hour specimens of urine of normal adults were diluted to 3000 c.c., and decreasing amounts were added to a series of tubes, the amounts decreasing by mathematical progression; each tube further received 2 c.c. of H_2O and 2 c.c. of a 0.1 per cent. solution of soluble starch; after incubation at 38° C. for half an hour the tubes were rapidly cooled and tested by adding a few drops of $\frac{n}{50}$ iodin solution; the limit taken was the tube just before the first tube in which blue is seen. Brown and Smith, as a result of their observations, conclude that the diastase content of normal adults falls within quite definite limits; marked decrease in the amount, in the absence of renal diseases, is strongly suggestive of some pancreatic disturbance, but such a finding is not diagnostic *per se*. The chief value of knowing normal values will be in furnishing criteria for testing renal function.

Functional Diagnosis of the Spleen with Adrenalin.—In some previous work Frey (*Zeit. f. d. ges. exp. Med.*, 1914, iii, 416) was able to demonstrate a definite marked lymphocytosis, coming on within a certain period of time after the injection of adrenalin. The present work attempts to determine where the adrenalin makes its point of attack, and whether, as was assumed, the increase in the lymphocytes is due to a mere mechanical heaping up of the cells. The effect of adrenalin injections was noted in animals before and after extirpation of the spleen in humans suffering from diseases of the lymphocyte-producing organs and after splenectomy. In puppies adrenalin apparently acts upon the smooth muscle of the spleen and causes a squeezing out of lymphocytes into the blood; in dogs, similar injections seemed to exert no influence upon the blood-picture; and in guinea-pigs, the resulting lymphocytosis stands in no relation to the spleen. In human beings suffering from lymphosarcoma and allied diseases, adrenalin causes a rise in lymphocytes equally as marked as in normals; in these cases where lymphatic destruction is going on, Frey asserts that the lymph glands cannot be the seat of production. In diseases of the spleen its cellular content is of much significance for the occurrence of adrenalin reactions; thus in Banti's disease practically no lymphocytosis occurs; on the other hand a good reaction occurs in cases of chronic hemolytic jaundice in which the structure of the splenic follicles is normal. Adrenalin causes a pronounced rise in cases of leukemia, lymphocytes almost exclusively of the lymphatic types, but myelocytes as well in the spleno-

medullary forms. The spleen was removed in a case of congenital hemolytic jaundice, which previously had shown a positive adrenalin reaction. For a time after splenectomy no reactions were induced but untimately they recurred. Frey inclines then to the view that adrenalin lymphocytosis is essentially a splenic reaction possessing considerable diagnostic importance.

Pancreatitis not Biliary in Origin.—In reviewing the literature of 250 cases of chronic pancreatitis SALLIS (*Rev. de chirurg.*, 1914, xxxiv–xxxv) was able to find only 50 which were not of biliary origin. The present paper is an analysis of these cases which occur usually in the female sex. They are caused, so far as is known, by no particular organism, but may occur in the course of most any general disease, and especially during pregnancy or secondary to trauma. Infection, contrary to the biliary cases which are usually lymphatic in origin, occurs through an ascending process in the ducts or by way of the blood-stream. Atrophy or hypertrophy may result, but in either case the gland becomes unusually hard. The disease generally commences with mild symptoms which invariably become worse or occur in attacks of increasing frequency. In either case the symptoms ultimately become continuous and lead sooner or later to death. Several clinical forms may be recognized. When the entire gland is affected, as was the case in 27 out of the 50, the prominent feature is attributable to the lack of the pancreatic digestive juices; when only the head of the gland is involved, jaundice and severe digestive upsets are common. The most valuable symptoms are pain, which is variable in intensity and location, emaciation, vomiting, and jaundice, and finally evidences of the disfunction of the gland, which is generally early in appearance. Glycosuria is but rarely present, and the Cammidge reaction is useless. The stools contain much fat in various forms, undigested muscle fibers, and cell nuclei. The diagnosis from carcinoma is made only with much difficulty and uncertainty. The most frequent complications are inflammation of adjacent viscera, portal thrombosis, cystic or malignant degeneration of the gland itself. Surgical treatment is the only one, and if instituted early, gives good results; symptoms vanish almost immediately, but in many instances healing of the wound is a matter of considerable time.

On the Finding of Diphtheria Bacilli in the Internal Organs in Fatal Cases of Diphtheria.—LIEDTKE and VOELCKEL (*Deutsch. med. Wochenschr.*, 1914, xl, 594) have examined the internal organs of seven children dying of diphtheria for diphtheria bacilli. In their cultural studies they have employed Conradi's medium. The results in all cases were the same. Diphtheria bacilli were abundant in the heart, lungs, liver, spleen, kidneys and bone marrow. In two cases they were able to examine the brain and in each they obtained positive cultures. The organisms recovered were typical morphologically and tinctorially. They were virulent, killing guinea-pigs in ten to forty-eight hours. In the experimental animals the characteristic changes were found postmortem, that is, redness and swelling of the adrenals, hemorrhages into the fat of the pancreas, infiltration at the site of inoculation and punctate hemorrhages in the intestine. Confirming the findings of Conradi and Beirast, the authors report that of thirty urines from diphtheria

patients, they found diphtheria bacilli in six instances. These cultural studies show that in severe "septic" cases of diphtheria it is not only the intoxication, but also the actual invasion of the body with the organisms that one has to deal with.

The Abderhalden Test in Infectious Diseases.—E. VOELKEL (*München. med. Wchnschr.*, 1914, lxi, 349) has applied the Abderhalden test to the study of diphtheria, anthrax, and typhoid infections, as well as to infections with trypanosames and spirochetes. Substrata of the bacilli were prepared by suspending the organisms in water, boiling and then testing the filtrate until no color reaction occurred with ninhydrin. Trypanosomes were obtained by infecting guinea-pigs with nagana, bleeding the animals, and collecting the blood in normal salt solution, to which 1.5 per cent. sodium citrate was added. On centrifuging, the trypanosomes collected above the red corpuscles and were removed. Spirocheta pallida could not be obtained entirely from culture medium. The organism was grown on horse serum. In the experiments with the Spirocheta pallida controls were used by boiling up the medium alone and using this as an additional substratum. The sera for study were obtained from experimental and human infections. All the luetic sera were human. In all of the infections studied the Abderhalden reaction appeared to be entirely specific.

Experimental Purpura Caused in Animals by the Introduction of Anti-blood Plate Sera—LEDINGHAM (*Lancet*, 1914, clxxxvi, 1673) found that it is possible to produce in guinea-pigs by the introduction of anti-blood-plate serum a disease similar to purpura. The serum is obtained by immunizing a dog against guinea-pigs' blood platelets, since it has been found difficult to secure platelets in sufficient amounts from human beings. Some 20 to 30 guinea-pigs are bled for a total of 150 to 250 c.c. of blood, and this is placed in two or three volumes of sodium citrate solution in normal saline. This is centrifuged and the cloudy supernatant fluid is obtained, which contains the platelets and a few erythrocytes. After centrifuging a few more times a serum free from corpuscles is secured and this is used for immunization. In all seven to eight injections are given at intervals of six to eight days, and the dosage used is 0.5 c.c. of platelets in normal saline. The immune serum always agglutinates guinea-pig platelets in the test-tube. When injected into guinea-pigs (1.5 c.c.) collapse and death occur in about one and one-half hours; autopsy reveals the presence of free blood in the peritoneal and pleural cavities, and the heart's blood contains completely agglutinated red corpuscles. After two intraperitoneal injections an animal of 500 grams died in four days. Section showed many subcutaneous hemorrhages in the intestinal mucosa, free blood in the peritoneum. Subcutaneous injections likewise cause death in three or four days, at which time there are numerous petechiæ in the skin, lungs, diaphragm, epicardium, and serous coats of the intestines.

The Dual Source of Cerebrospinal Fluid.—WEED (*Jour. Med. Research*, 1914, xxxi, 21, 51, 93) concludes from previous observations, recorded in the same journal that there are several pathways of escape for the spinal fluid: (1) it may reach the major circulation by passage

into the sinuses from the arachnoidal villi; (2) there probably is some drainage by way of lymphatic channels; (3) there may be some retrograde passage from the venous system into the subarachnoid space. No evidence was obtained of the escape of spinal fluid into the cerebral veins or capillaries. During the work upon which these observations were made, studies were carried on in the hope of producing genuine evidence for the growing idea that spinal fluid is a product of the choroid plexus and of the nervous tissue itself. Evidence of a convincing nature was obtained as to the choroid origin of spinal fluid. A new technique was devised whereby ventricular catheterization could be carried out without there being any admixture of the products of the perivascular system. Moreover, the operative procedure was so improved that the usual condition of low arterial blood-pressure at the time of catheterization was eliminated. A new detail was the standardization of the resistance to flow in the catheters employed. When such a catheter is in place, fluid continues to flow for several hours, cessation being due presumably to an exhaustion of the choroid plexus. The second phase of the problem was attacked by means of a new method of the subarachnoid injection of ferrocyanide solution. Provided such injections are made under suitable pressure conditions, the perivascular spaces around the veins and arteries are heaped up with Prussian-blue granules. This along with other evidence leads the authors to conclude that the fluid obtained by lumbar puncture represents not only the secretion of the choroid plexus, but also the fluid waste products of nerve-cell activity, poured into the subarachnoid space by way of the perivascular channel.

The Cultivation of the Causative Agent of Rabies—H. NOGUCHI (*Berlin. klin. Woch.*, xli, 1931) reports the successful cultivation of the causative agent of rabies. The culture medium employed was that which he had used successfully in the cultivation of the spirochete of relapsing fever. Some of the inoculated tubes remained sterile, others were contaminated, but in many the organism grew in pure culture. It has been possible to carry it through as many as twenty-one generations. Microscopic examination of the virulent cultures showed nothing; microscopic examination, however, revealed the presence of numerous granular chromatin bodies of varying size. Some were scarcely visible; the larger bodies measured 0.2 to 0.3μ. Groups of very small pleomorphic chromatin bodies, measuring 0.2μ to 0.4μ wide and 0.5 to 4.0μ long, were also noted. They stained red or bluish with Giemsa's stain. On four occasions Noguchi observed the development of bodies with a single round or oval nucleus surrounded by a membrane; these arose in cultures which originally contained only the granular or pleomorphic bodies. The nucleated bodies were numerous and of varying size (1 to 12μ), and were observed singly or in groups of two, three, four or more cells. The nuclei were stained dark blue or violet with Giesma's stain, the cytoplasm azure, and the membrane reddish. Certain of these bodies were in every particular identical with Negri bodies. Inoculations of rabbits, guinea-pigs, and dogs with cultures which contained granular bodies or granular and nucleated forms produced typical rabies.

SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

FORMERLY JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA AND SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

The Abbott Treatment of Rigid Scoliosis with a Report of Sixty Cases.—KLEINBERG (*Amer. Jour. Orthop. Surg.*, 1914, xii, 134) says that 18 cases gave up the treatment during the first six months; seven of this number discarded the jacket during the first few days while the rest were observed from three to six months. In all instances it was the discomfort, restlessness, and pain incident to the treatment that caused the patients to discontinue it, although these patients were willing to undergo a great deal of inconvenience for the hope of improvement. The remaining 42 cases are divided into five groups. The first includes 8 cases, all of the severest type, presenting without exception "razor backs." In none of these did the treatment produce any appreciable improvement. The second group, including 10 cases, had all very advanced and rigid deformities, the curve of the spine being S-shaped in every instance with the two parts of the curve almost equal. When the treatment was interrupted every patient was satisfied and there was improvement, in some very marked, in the external appearance. However, the conditions of deviation and rotation of the vertebræ, as judged from the Roentgen-rays, either remained unaltered or in some cases seemed to change for the better while the patient was in the jacket, but relapsed a short time after it was removed. One cannot, therefore, predict whether the improvement noted will be permanent. The third group, including 8 cases, all had severe deformities with marked rotation and deviation of the spine, but the dorsal curve was either the only one or was the more prominent with a slight compensatory curve. In this group there has been no complete correction of the deformity but there has been an unusual and very decided improvement in the external appearance and in most instances an actual partial reduction of the deformity of the spine, as shown by the Roentgen-ray. In the fourth group, of 10 cases, the deformity was rigid and varied from mild to severe types. In every instance there was marked improvement in the external appearance but especially in the Roentgen-ray findings. As most of these patients are still wearing supports and under active corrective treatment, a final report is impossible. The fifth group, of 6 cases, all had mild curves of moderate degree. Of these, two were greatly improved, two apparently corrected, and two apparently overcorrected, but all of them have relapsed to

their original condition. Kleinberg reached the following conclusions: The Abbott jacket from its weight and shape and the pressure exerted on the body is at all times a severe tax to the patient. Aside from temporary indisposition and the discomfort of the pressure on the chest, anorexia, etc., incident to the treatment, no untoward results have been experienced excepting the hollowing of the chest which has remained permanent only in one instance. As might have been expected, it was found that the deformity even in its mildest form, did not yield rapidly to the Abbott treatment, and that it took many months to effect any real radical change. Of the 60 cases, 18, some of which offered hope of improvement, gave up the treatment; 8 were not improved at all, and 34 were definitely made better in external appearance with or without a definite change in the spine itself. Of this latter number, 6 cases relapsed. This method, therefore, is applicable to the milder degrees of rigid scoliosis, most of which the writer has seen improved, though he has not yet seen any case, no matter how mild, cured, *i. e.*, transformed into one with a perfectly symmetrical back.

Observations on Myeloid Sarcoma with an Analysis of Fifty Cases.—STEWART (*Lancet*, November 28, 1914, 1236) says that myeloid sarcoma is locally malignant and does not undergo dissemination. It is to be clearly distinguished, both clinically and pathologically, from malignant giant-celled sarcoma, in which death with visceral dissemination is the rule, even after the most radical treatment. The histological diagnosis it based on the morphological characters of the giant cells, especially as regards their nuclei. In myeloid sarcoma the latter are numerous, uniform, small, and without mitoses; in malignant giant-celled sarcoma they are few, sometimes single, irregular, and often very large, while mitotic figures are frequent. After investigating this comparatively large series of cases, and from study of the literature Stewart feels bound to advance a strong plea for the conservative treatment of myeloid sarcoma. Especially would he advocate thorough curettage as the operation of choice in the first instance in suitable cases; failing this, a local resection of the growth. Amputation should be the last resort, and only after the failure of less radical measures. An accurate histological investigation of the tumor in all cases is essential.

Operative Treatment of Acute Epididymitis.—SMITH and FRAYSER (*Annals of Surgery*, 1914, lx, 719) report their observations after reviewing over 300 cases in Ancon Hospital since 1908, in which operative treatment gave most gratifying results. They describe the operation at follows: After shaving the parts thoroughly they use a 3 per cent. alcoholic solution of iodine. External and parallel with the epididymis, an incision is made into the tunica vaginalis which should be large enough to deliver the testicle. Examine the epididymis and multiple punctures with a blunt probe in that portion which is inflamed. Gently massage the part, wash with warm salt solution and return testicle to scrotum. Close the tunica with catgut and insert a narrow iodoform gauze drain. The external wound is closed with silk-worm gut, using the subcuticular stitch—the drain passing out at the lower

angle. After operation apply a sterile gauze dressing and use a suspensory bandage to support the scrotum. On the second day the wound is inspected and the iodoform drain removed. Daily dressings are not necessary. Usually on the fourth day the patients are up and allowed the freedom of the wards. On the fifth day a 2 per cent. alcoholic solution of iodine is applied over the line of incision and the sutures removed, if silk-worm gut has been used. In the majority of cases patients return to work on the sixth day. Epididymoty is the rational thing to do because it shortens the duration of the disease; relieves the severe, weakening, sickening pain at once, causes the temperature to fall and induration to disappear rapidly. What is radical today is conservative tomorrow.

Genital Symptoms in the Diagnosis of Appendicitis.—Lanz (*Zentralbl. f. Chir.*, 1914, xlvi, 1705), after referring to the suggestion of Horn that the pain produced by dragging on the spermatic cord was a valuable sign, sometimes, in appendicitis, says that he found this symptom constant in four cases operated on. He also observed, from observations on a dozen cases, that the cremaster reflex was weakened or absent, and that frequently the right spermatic cord was thickened from collatereal edema in acute cases and exquisitely tender when it was rolled under the examining finger just after it emerged from the external inguinal ring, at the internal attachment of Poupart's ligament and external to the spine of the pubis. While the tip or end of the finger can be introduced into the external ring on the left side without trouble or pain, on the right side it detects the rigid lower border of the internal oblique and transversalis muscles which prevent further penetration into the canal. This rigidity is due to the same muscular defence which we recognize in the right rectus muscle in appendicitis. Lanx advises examination of the genital symptoms in the following order, a comparison being made with the left side: (1) Canal symptoms: (*a*) tension of the pillars of the external ring. (*b*) muscular resistance on pressing the finger into the inguinal canal. (*c*) pain produced by coughing while the finger is in the canal; (2) Spermatic cord symptoms: (*a*) pain on pulling the cord, (*b*) pain from pressing on the cord, (*c*) Swelling of the cord at the external ring; (3) Testicular symptoms: (*a*) cremaster reflex. Systematic comparison of these findings with those at operation will help us in deciding before operation the severity of the attack, the localization of the focus, its relation and its eventual extension to the peritoneum.

An Experimental Study of Osteogenesis.—Mayer and Wehner (*Amer. Jour. Orthoped. Surg.*, 1914, xii, 213) say that all four series of their experiments—transplants of periosteum, subperiosteal resections, cap implantations, and bone transplants—combined to emphasize the osteogenetic function of the specific-osteoblastic cells of the periosteum and the inability of the adult bone cell to form new osseous growth. Bone growth occurred in all the transplants of periosteum after subperiosteal resection; it was, however, absent in the cap experiments where the ingrowth of periosteum had been excluded. In the bone transplants, the adult bone cells of the grafts gave no evidence

of activity whereas the periosteum showed marked osteoblastic properties. Similar osteogenetic power was manifested by the transplanted endosteal cells lining the marrow cavity and the Haversian canals, provided their vitality was maintained by intimate union with the tissues of the environment. Bone macroscopically bare of periosteum can be successfully transplanted into the soft parts, not because the bone cells give rise to new bone formation, nor because of a metaplasia of the surrounding connective tissue cells into connective tissue osteoblasts, but because of adherent periosteal cells, and of living endosteal cells. The practical conclusions for the surgery of bone transplants are self-evident: bone should be transplanted with the periosteum; if feasible it should be split lengthwise, so at to insure an intimate union of the endostium with the surrounding tissue uses. Bone macroscopically bare of periosteum can, however, be transplanted with good hope of success if care be taken not to scrape away the adherent cells of the osteogenetic layer of the periosteum. The classical conception of the complete necrosis of the bony portion of the transplant must be modified, since, though the majority of the transplanted bone cells necrose, numerous cells can maintain their vitality until the graft has become vascularized. These cells, however, give no evidence of osteogenesis. The process by which the necrotic bone of the transplant is replaced by living bone consists not only in the usual sequence of lacunar absorption and subsequent bone apposition, but in a "creeping replacement." In this process the young bone cells, before they have assumed the adult form and before the bone has become lamellar in structure, show evidence of direct cell division, and of power to absorb necrotic bone and form new bone. The living osseous tissue advances into the old by the intercellular deposit of bone, also probably by a direct advance of the young bone cells in the old lacunæ.

Pott's Disease; Albee's Bone-grafting Operation; Results in a Series of Twenty-six Cases Operated More Than Six Months Ago.—Ryerson (*Amer. Jour. Orthoped. Surg.*, 1914, xii, 259) says that 21 of these 26 cases are apparently well in a minimum time of six months after operation. Five are at least distinctly improved and may possibly make complete recovery. Eleven more cases were operated on less than six months before the reading of the paper. In all of the 37 cases there was no mortality whatever. He thinks these results will bear comparison with those obtained under any other form of treatment as yet devised, especially when it is remembered that a majority of these patients had been long and patiently treated by consecutive orthopedic measures, and were operated on as a last resort. It is Ryerson's belief that the work must be done rapidly to be safe, rapidly but not hastily. A motor saw is a practical necessity for the saving of time and for the accurate cutting of the splint. The splitting of the spinout process must be carefully done and can be done with a narrow chisel better than with the broad ones which are now in fashion. No attempt need be made to split the shafts of the spinous processes in children, for they are too thin to be split by any operator. The most that one can do is to split the tips and strip off the periosteum along one side of the shafts. The muscle and periosteum should not be stripped from the opposite

side of the spinous processes, as the bone needs all the blood supply it can get. The splint should be sewed in with heavy braided silk sutures, boiled in bichloride and then in paraffin. These sutures should be strongly placed in the deep tissues or in the tips of the processes themselves, if it is desired to make any correction in the deformity, In three of his cases one or two of these sutures came out a few montht after operation, without marring the result in any way. Kangaroo tendon is unreliable under the tension which he uses. A needle-holder is a necessity in placing the sutures sufficiently strongly. In most cases a considerable correction of the deformity can be and should be obtained. The point of greatest importance is to make a splint that will extend well above and below the diseased vertebræ. It is not too much to have it go at least three vertebræ above and below the limits of the disease, if this is possible to accomplish. It is far better to immobilize several vertebræ too many than one vertebra too few.

Some Practical Considerations in the Diagnosis and Treatment of Abscess of the Cerebellum.—MILLIGAN (*British Med. Jour.*, November 14, 1914, 833) says that the decades from 10 to 20 and from 20 to 30 provide the greatest number of cases of abscess of the cerebellum. Males are affected twice as frequently as females, and abscess on the left side is twice at frequent as abscess on the right side. The great majority of chronic cases are secondary to labyrinthine suppuration, the aqueductus vestibuli being the actual route of infection in 30 per cent. Of the clinical indications of cerebellar disease, nystagmus is one of the most important. In labyrinthine suppuration it is first directed toward the affected side and subsequently toward the sound side. It remains toward the sound side throughout the course of the disease and decreases *pari passu* with the destruction of the labyrinth. Cerebellar nystagmus is directed first towards the sound side and subsequently toward the affected side. It increases with the progress of the suppuration within the cerebellum. To test the function of the labyrinth the caloric test is the most convenient and can be applied with the patient sitting up or lying in bed. To fix the position of the eyes a geniometer it useful. Speaking generally, exploration of a cerebellar abscess should be made through the posterior antral wall in the space between the interauditory meatus and the sigmoid sinus groove. Counter drainage behind the "groove" is a valuable measure and much facilitates after-treatment. Prior to operation the withdrawal of a small quantity of cerebrospinal fluid is advisable to lessen existing intracranial tension and to prevent sudden respiratory or cardiac failure. For the drainage of chronic abscesses the author uses a special form of drainage tube, a tube within a tube, so that the inner tube may be removed without disturbing the position of the outer tube. He operated on 27 cases in the past ten years, 17 being in males and 10 in females. Seven were on the right side and 20 on the left side. Seventeen were cured and ten died.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

The Use of a Series of Vaccines in the Prophylaxis and Treatment of an Epidemic of Pertussis.—Hess (*Jour. Amer. Med. Assoc.*, 1914, lxiii, 1007) reports on the use of a series of vaccines in an epidemic of pertussis occurring in an institution for young children. He found that none of the four vaccines, including an autogenous strain, was of value in curing or tempering the disease. That this failure was not due to tardy inoculations is emphasized by the fact that many of the severest cases received not only early active treatment but also prophylactic vaccination. No other conclusion seems possible from a review of the epidemic of 85 cases and a comparison of the severity of the disease among the vaccinated and the unvaccinated. This opinion is based solely on his experience in this epidemic and does not preclude the possibility that a different dosage of vaccine or treatment with a modified vaccine, may not prove to possess curative properties. The use of the vaccines in prophylaxis seemed to offer greater promise in view of the established fact that other vaccines, for example the typhoid vaccine, possess prophylactic although no curative power. This seems to some extent, although to a far less degree to be true of pertussis vaccine. In view of the fact that twenty children developed pertussis in spite of the prophylactic treatment, we cannot compare its protective value to that of typhoid vaccine. However, the proportion of unvaccinated children who developed pertussis so greatly exceeded the number of the vaccinated who developed the disease, that we conclude that the vaccine has protective value in a certain percentage of cases, and that it should be employed in institutions and in families to prevent the spread of this infection.

The Action of Potassium and Sodium Iodid and of the Iodin Ion on the Heart and Bloodvessels.—Macht (*Johns Hopkins Hosp. Bull.*, 1914, xxv, 278) says that the rationale and the scientific basis for the use of the iodids are very inadequate and he endeavored to obtain more exact knowledge of their action by experimental work. His work was chiefly directed to the effect of the iodids upon the circulatory apparatus. His experiments indicated that the potassium ion produces a relaxation of the bloodvessels and a marked depression of the heart; that the sodium ion has a slightly stimulating action on the bloodvessels and also stimulates the heart, and the iodin ion is a powerful stimulant to both the heart and bloodvessels, as shown by its action in experiments on isolated organs. The stimulating effect of the iodin ions however is greatly inhibited in the intact animal by their chemical combination with the protieds of the blood. Whether the chemical compound thus produced in a stable

one or whether it is a loose one and slowly breaks up, setting iodin free, remains an open question. If iodin is set free a stimulating effect is to be expected. The action of sodium and potassium iodid on the heart and vessels can be best understood from the action of their component factors. Sodium iodid possesses no depressing property for the sodium ion is a vascular constrictor and a cardiac stimulant, and the iodin ion insofar as it is free to act has the same action. Potassium iodid on the other hand, clearly shows the depressing of the potassium ion on the heart and vessels, especially of mammals, not only on isolated organs, but also in the living animals. It is therefore no a matter of indifference which of the iodids is to be chosen for the purpose of depressing the circulation as, for instance, in the case of an aneurysm. Macht says that so far as experimental evidence goes the iodids possess no special virtue of lowering the blood-pressure, but that effect is really due entirely to the potassium and could be produced even more efficiently by other potassium salts.

Active Immunization in Diphtheria and Treatment by Toxin-Antitoxin.—Park, Zingher, and Serota (*Jour. Amer. Med. Assoc.*, 1914, lxii, 859) say that the property of toxin-antitoxin mixtures to produce immunity in animals has long been known. In 1913, Behring published the results obtained in human beings. The combined substances were either neutral or slightly toxic to the guinea-pig. Individuals were injected with small doses (from $\frac{1}{20}$ to $\frac{1}{10}$ c.c.) which were repeated in from seven to ten days. The first injections were made subcutaneously or intramuscularly, while later the intracutaneous administration was favored, since the more distinct local reaction was believed to induce a greater efficiency of vaccination. The results as reported from different observers have not been uniform, and as a rule are not distinctly stated. Hahn reports antitoxin production in 36 out of 40 treated, but the fact that 25 of the 40 had natural antitoxin already present modifies greatly the favorable nature of this result. The immunizing response to vaccine varies widely. It seems greatest in young adults and Zangmeister reports the interesting fact that the newborn are nearly a hundred times less susceptible to vaccine than adults. Kissling reports results in the immunization of 310 patients who were exposed to infection. In the 111 who were injected twice no diphtheria developed. In the 109 cases injected once, 8 patients developed clinical diphtheria. During an epidemic of diphtheria, Hahn and Sommer vaccinated part of the inhabitants of several villages: of 633 patients considered fully immunized only two developed mild diphtheria, but 10 of the group developed it during the first ten days. The disease continued to spread to some extent among those not vaccinated. Bauer finds that the persistence of the bacilli in carriers is not shortened by active immunization. He believes that not only all patients with antitoxin, but also those without natural antitoxin can be immunized, if sufficient doses and amounts of vaccines are injected. The interval between the injections of vaccine and development of antitoxin varies in different cases. According to Hahn it is usually not less than three weeks. Kleinschmidt and Viereck found it shorter—even eight days. Patients with natural antitoxin usually show early and considerable antitoxin production. They also generally

show a somewhat greater local susceptibility to vaccines. This, according to von Behring, is due to sensitization from previous infections with the Klebs-Loeffler bacillus. According to von Behring, the higher temperature of fever will destroy antitoxin at an increased rate so that an amount of antitoxin, which generally protects, fails to do so in measles and scarlet fever. Schick and Karasawa find, however, that no change in antitoxin content is caused by measles. Von Behring considers that 0.01 unit per cubic centimeter is sufficient to protect healthy persons. Much less than this probably suffices except under unusual conditions, as in scarlet fever. During the past twelve months the attempt has been made to immunize actively against diphtheria the patients in the scarlet fever wards of the Willard-Parker Hospital. For this purpose mixtures of diphtheria antitoxin and toxin were prepared, either slightly antitoxic, neutral or slightly toxic to the guinea-pig. The injections were made subcutaneously or intramuscularly in doses of from 0.25 to 1 c.c. of undiluted vaccine; a few of the non-immune persons received as high as from 3 to 5 c.c. at each injection. The dose was repeated two or three times at intervals of from three to seven days. The injections were made posteriorly in the intrascapular region, in some over the insertion of the deltoid. The local reactions consisted as a rule of varying degrees of redness, induration, pain and tenderness; in part they seemed to depend on the size of the dose and in part on the individual susceptibility. Persons with natural antitoxin gave somewhat more frequently the stronger local reactions. The constitutional symptoms were as a rule rather mild, occasional temperature reactions of from 1 to 3 degrees were noted after larger doses of the strong vaccines. The authors found that active immunization produced a very decided increase of antitoxin in a relatively short time in all persons who had natural antitoxin. These, however, were immune to diphtheria before the injections were made. In a series of 700 scarlet fever patients tested by them for natural immunity by the Schick reaction, 400 gave a negative reaction. 57 per cent. were, therefore, naturally protected and needed neither active nor passive immunization. Less than one-quarter of the remaining 43 per cent. which were probably susceptible to diphtheria, reacted to active immunization with mixtures of diphtheria toxin and antitoxin to a degree sufficient to immunize them. A larger percentage developed a trace of antitoxin which was possibly enough to give a slight protection. In their conclusions they say that those who are definitely exposed to infection should be passively immunized even if the toxin-antitoxin injections have been given. The use of the Schick test will eliminate the necessity of immunizing about two-thirds of those exposed, as those not reacting are probably immune. This natural immunity probably continues for a considerable period of time, possibly indefinitely. Active immunization is indicated when there is no immediate danger of infection and when it is desirable to lessen the number of susceptible persons. It is too early to decide whether active immunization should be attempted on a large scale. The lack of a sufficient response of at least 50 per cent. of those susceptible to diphtheria and the fact that the immunity lasts for but one or two years are drawbacks that will probably limit its usefulness.

The Present Status of Organic Iodin Preparations—McLean (*Jour. Amer. Med. Assoc.*, 1914, lxiii, 1382) says that the larger number of commercial preparations of organic iodin resolve themselves naturally into two classes: (1) iodin products of the higher fats or fatty acids and (2) iodized albumins. The chief iodized fats and fatty acids on the market at the present time are iodifin, sajodin, and iodinal. The preparations contain varying amounts of iodin but are sufficiently similar in their characteristics to allow of their being considered together. The advantage over the alkaline iodides claimed by the manufacturers are chiefly as follows: (1) absence of gastro-intestinal irritation, (2) slower absorption, (3) longer retention in the body and a more uniform rate of excretion, and (4) less tendency to produce iodism. The first claim is in general well substantiated, as all of these substances are bland and unirritating, the iodin being so firmly bound as to be inactive locally. These substances are absorbed without much change in their composition, the absorption being similar to that of fatty acids. While 75 per cent. of the iodin given in the form of potassium iodid is excreted in the urine within twelve hours, and the highest amount in the urine is in the second hour, the absorption and elimination of the iodized fats is much slower. When sajodin is given, iodin does not appear in the urine until after from one to three hours, and while the highest point in the excretion is reached within twelve hours the amount excreted remains high for thirty hours, giving a much more uniform rate of excretion. The iodin is excreted in inorganic form and probably is effective in the body only after it is separated from its organic molecule. The fact that relatively more iodin is found in the nervous tissues probably has little bearing on the efficiency of these substances in cerebral syphilis as their lipoid solubility would not favor their entrance into syphilitic tissue. The lessened tendency to iodism claimed by many observers may be explained by the slower and more uniform release from the lipoid combination in the form of available iodin. Where continuous small amounts of iodin are desired, as in arteriosclerosis, bronchial asthma, lead poisoning, etc., this iodin may be supplied in a form non-irritant to the stomach as an iodized fat or fatty acid, and the probability of iodism would not be great. When large amounts of iodin are desirable, as in cerebral syphilis, etc., the therapeutic effect seems to depend on the same property that causes the toxic effect, that is, the high concentration of iodin, and any effort to decrease the concentration would result in a loss of therapeutic efficiency. The iodized albumins on the market are chiefly iodalbin and iodo-casein. They are relatively unstable and iodalbin contains some free iodin and much more easily available iodin. The absorption of iodin is somewhat retarded and these preparations are less irritant to the stomach than the soluble inorganic salts. Iothion and iothion oil are recommended for local applications and for percutaneous administrations. They are apparently efficient in case percutaneous use is desirable. Another class of preparations, the iodized tannins, are not strictly organic preparations. They are prepared in the form of wines or syrups, and contain tannin with a small amount of loosely combined iodin. They decompose rapidly in the stomach and their action is the same as that of a corresponding amount of potassium iodide.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND FREDERICK O. WAAGÉ, M D.,

OF PHILADELPHIA.

The Epifascial Neosalvarsan Injection of Wechselmann in Children.—HANS KERN (*Berlin klin. Woch.*, 1914, li, 1742) describes the method as used in an orphanage in Berlin. The combined treatment has been employed for some time, and besides the exhibition of mercury in some acceptible form, from four to six injections of neosalvarsan are employed. The use of neosalvarsan alone was discontinued because the results were not permanent enough. On account of the difficulty of giving neosalvarsan intravenously in children, especially between the second and seventh years, the epifascial method of Wechselmann was adopted and has proven very satisfactory. This method consists of depositing the solution exactly upon the fascia. The guide to this location is a sensation of roughness felt on drawing the tip of the needle over the fascia. This sign. however, frequently fails in children owing to lack of development in the fascia. The concentration of the solution of neosalvarsan was gradually increased during the application of this form of treatment from month to month until 100 per cent. solutions were being used. Infiltration of tissue followed the procedure at first but with increasing skill in technique gradually disappeared until in a series of 88 injections but 3 cases showed slight infiltration. The conclusion was that it was the technique and not the concentrated solution that caused infiltration. The method is naturally more difficult with small children than with adults, and the impression frequently was that the epifascial injection had become really an intramuscular one. However, the expected infiltration did not appear. No clinical difference was noted in the action of the intravenous and epifascial method; the latter, however, has a slower, steadier action and avoids the sudden stormy flooding of the intravenous method. The author recommends the epifascial method in children. It takes the place of intravenous injection and infiltration disappears or diminishes with improvement in technique, which, if not simple, can easily be learned.

Vaccination against Varicella.—KLING (*Berlin klin. Woch.*, 1915, lii, 13) gives his technique and results in vaccinating against varicella. During an epidemic of varicella KLING began to vaccinate healthy children against the disease and found the reaction very slight, the efflorescence almost invariably limited to the point of vaccination and the fever and constitutional signs absent. From a practical standpoint it was significant that all children successfully vaccinated remained immune to the contagion of the disease. In all there were 135 cases vaccinated, only 45 of which failed to give a good positive reaction. In 10 cases a few vesicles appeared on the body, besides the local reaction, and in 3 cases the vesiculation was more general, in all the others

the reaction was localized. All of the 135 cases with positive reactions remained free from the contagion during months of observation, while in 108 children who were unprotected or in whom the vaccination had failed to "take," 73 per cent. contracted the disease. It therefore appears that this process of vaccination is of utility in protecting against the severe forms of varicella. The technique of vaccination against varicella follows the main principles in all vaccination, in that the child from whom the vaccine material is taken should be free from syphilis and tuberculosis and be normally healthy. The operation in all respects should be aseptically performed. The vesicle from which the serum is derived should be from a fresh crop, contain clear serum, and should not be surrounded by a marked inflammatory areola. The vaccination-lance is preferred to the Pirquet needle. The skin on the arm is prepared in the usual manner, the lance is inserted into the vesicle, so that the serum covers the point and a light stab is made on the prepared skin surface, deep enough to slightly draw blood. About three stabs are made, then the lance tip is again covered with serum from this vesicle and three more stabs are made. It has been shown that where one or two stabs only are made, only a small percentage of reactions occur. Usually the reaction will occur in only one or two of the stabs, the rest remaining negative. A sterile dressing is applied for two days when it is removed as the punctures will have healed. As soon as the reaction sets in the sterile dressing must be again applied to prevent secondary infection.

GYNECOLOGY

UNDER THE CHARGE OF
JOHN G. CLARK, M.D.,
PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Diathermy in the Treatment of Pelvic Inflammation.—The noted Spanish gynecologist, RECASENS, in an article recently contributed to one of the German journals (*Monat. f. Geb. u. Gyn.*, 1915, xli, 130) says that the "operative madness" which prevailed during the last twenty years of the past century and the first few years of this, with regard to the treatment of inflammatory conditions of the adnexa is gradually giving place to more conservative and rational methods. It has been conclusively demonstrated that many cases which were formerly considered only fit subjects for radical surgery may, if properly treated, attain at least a complete symptomatic cure without operative interference. The best of the conservative methods, in his opinion, is the application of heat, for the purpose of inducing hyperemia, which latter is as effectual in causing resolution of chronic inflammatory processes in the genital organs as it is in the Bier treatment of joints, etc. In the past, however, great difficulty has been experienced in actually applying an efficient quantity of heat to the internal genital

organs; the various methods by which this was attempted, such as hot applications, douches, and even abdominal and vaginal electrically heated coils, were all more or less unsatisfactory, in that they were not able to drive the heat into the deeper tissues, where it was wanted. These difficulties are entirely overcome, however, in RECASENS' estimation, by diathermy, in which process an electrical current, which can be passed accurately between two electrodes placed in any desired positions, and whose strength can be absolutely regulated, is transformed in the tissues through which it passes from electrical to heat energy, thus applying the latter along its whole course. For most purposes, RECASENS employs a large electrode in the lumbosacral region, and another on the lower abdomen, passing the current from the latter to the former, and thus exciting a condition of hyperemia in all the pelvic organs. In other cases, the dorsal electrode is replaced by one in the vagina; it must be large enough practically to fill up the entire vagina, and in this case the current is sent from the vaginal to the abdominal electrode. When working in this way, the strength of current must be considerably less than when both electrodes are on the external surface. The current must be so regulated that the heat development takes place slowly but progressively, and that it is maintained at its height for thirty to forty minutes. RECASENS says his best results with this method of treatment have been obtained in cases of chronic salpingo-oöphoritis with adhesions; in a few sittings he has seen the formerly fixed uterus become movable, the pains disappear, and exudate, where present, absorbed. In chronic inflammatory processes associated with pus formation, however, he has seen practically no benefit, either subjectively or objectively. While unable to offer any positive explanation for the results secured, the author ventures the opinion that possibly the heat has some effect in inhibiting the growth of pathogenic organisms in the infected tissues.

Nerve Distribution in the Ovaries.—In a very elaborate series of investigations, WALLART (*Ztschr. f. Geb. u. Gyn.*, 1914, lxxvi, 321) has studied by means of special staining technique the distribution of nerve fibers in human and various types of mammalian ovaries. He finds that the nerves enter the ovary at the hilus in the form of large, very tortuous bundles, the great tortuosity being evidently a provision to allow for changes in the size of the ovary incident to ovulation. Gradually giving off branches to the stroma, the nerve bundles eventually reach the cortex, where they break up into such an enormously rich network of fibers that in suitably stained specimens this region of the ovary appears to consist in large part of nerve tissue. There is also an exceedingly rich nerve supply to the walls of bloodvessels throughout all portions of the organ. An interesting relation was noted between the nerves and the Graafian follicles; while these are completely surrounded by a rich network of fibers, no penetration of nerves could ever be demonstrated within the epithelial portion of the follicle, *i. e.*, within the membrana granulosa, which tissue, together with the developing ovum, appears to be without direct nerve connection. A few fibers were found in mature corpora lutea, but only in the connective-tissue septa containing the bloodvessels—never running between the lutein cells. After degeneration and retrogression of the

corpus luteum sets in, however, nerve fibrils can often be seen in close relation to the individual cells. This late appearance of nerves in the corpus luteum may be due, WALLERT thinks, to faulty technique the large amount of fat in the fresh corpus luteum seriously interfering with the staining reactions, and thus preventing satisfactory demonstration of nerve fibers, or it may stand in some relation to the gradual evolution of what he considers a true "interstitial gland" from the remains of the corpus luteum. At any rate, WALLART always found an exceedingly rich network of fibers associated with the terminal stages of this structure, even including the apparently inert mass of connective tissue known as the corpus fibrosum, which represents the terminal form of the extinct corpus luteum. He thinks, therefore, that even this structure has a distinct secretary function, by which the ovary is to some extent brought into relation with other ductless glands. Although not able to demonstrate positively the presence of ganglion cells in the ovary, WALLART discovered numerous bodies so strongly suggestive of them as to warrant the belief that in all probability ganglionic elements are in reality present.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.,

LECTURER ON PATHOLOGY AND CLINICAL MEDICINE, MC GILL UNIVERSITY, MONTREAL; SOME TIME PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF VERMONT, BURLINGTON, VERMONT; SENIOR ASSISTANT PHYSICIAN, ROYAL VICTORIA HOSPITAL, MONTREAL,

AND

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY AND BACTERIOLOGY, UNIVERSITY OF PITTSBURGH, PITTSBURGH, PA.

Cholesterin in Blood.—MILKOWITSCH (*Russki Wratsch*, 1911, xxii) determined in a number of experiments the influence of cholesterin, lecithin, adrenalin, and other substances upon the process of phagocytosis. He used the Wright method. He employed the Staphylococcus aureus and tubercle bacillus in conjunction with normal human serum and leukocytes. He comes to the conlcusion that both cholesterin and lecithin increases the phagocytosis of Staphylococcus aureus and tubercle bacillus. ROEHMANN (*Berlin klin. Woch.*, 1912, No. 42) found in the red blood cells, but not in the blood plasma, an enzyme which acting like a lipase splits the cholesterin-ester. He calls it a cholesterase. It is important to determine whether other tissues contain this cholesterase and whether an increase of cholesterin ester in amyloid kidney and in arteriosclerosis has a relationship to this ferment. It is suggested that the accumulation of cholesterin in the liver is associated with the cholesterase of the red blood cells which are destroyed by this organ. The deviation of the complement in the

Wassermann reaction is enhanced by the presence of cholesterin. It would appear that the sera giving a positive Wassermann contained more cholesterin than others. It may be that this increase is directly related to an excess amount of cholesterase in the serum. CITRONBERG (*Biochem. Zeitsch.*, 1912, xiv, 281) has shown that the blood of horses is capable of decomposing cholesterin-esters without the addition of liver extract. This decomposition does not take place in serum alone, but it appears that the cholesterase is contained within the red blood cells. It is indicated, in fact, that the red cells not only contain the cholesterase but also the cholesterin-ester. PRINGSHEIM (*Münch. med. Woch.*, 1912, 1757) reports the case of a man, aged thirty-four years, who after a severe cold developed hemoglobinuria without marked change in the blood picture. The Wassermann was positive. Mercurial treatment was of no value. The patient then received five injections of 0.05 grms. of cholesterin in a 10 per cent. emulsion intramuscularly in a period of eleven days. The hemoglobinuria disappeared. After eight days he had another attack as severe as original. The resistance of the red blood cells was normal to saponin solutions. BUERGER and BEUMER (*Berlin. klin. Woch.*, 1913, No. 3) studied the lipoid content of the blood. The greatest cholesterin and lecithin values of the serum was observed in diabetic lipemia and cholemia. In a case of eclampsia they also found an increase. Less than the normal quantity was found in pernicious anemia, chlorosis, malignant cachexia, and in inanition. It is true that others have stated to have found an increase under conditions similar to these. A constant relationship, therefore, is not necessarily found in given diseases since the content in lipoids is influenced by the diet and the nutrition of the patient. In every serum some free cholesterin was found, equaling about 30 per cent. of the fats present. KANDERS (*Biochem. Zeitsch.*, 1913, lv, 96) used the method of Windaus and determined the cholesterin content of the serum of the horse, dog, cow, rabbit, guinea-pig, and sheep. He found the cholesterin content to increase in the following order: cow, horse, dog, sheep, guinea-pig, and rabbit. In the order of cholesterin or cholesterin-ester content of the red blood cells, are dog, guinea-pig, rabbit, cow, and sheep. He found that human sera with positive Wassermann reactions had a lower cholesterin ester content than the negative. OBAKEVITSCH (*Russki Wratsch*, 1913. No. 30) determined the cholesterin content of blood by the colorimetric method of Grigaut. The cholesterin content in a litter of blood serum normally varies from 1.4 to 1.8 grams. A fatty diet readily increases the cholesterin content. Hypercholesterinemia was found in pregnancy, nephritis, cholelithiasis, arteriosclerosis, lues, and during convalescence from acute infections. On the other hand, hypocholesterinemia was found in acute and subacute infections, anemias, and hemolytic jaundice. GAUCHER and DESMOULIER (*Bull. de l'Acad. de Med.*, Paris, 1912, No. 26) found a striking parallelism between the cholesterin content of the serum and the Wassermann reaction. CANTIERI (*Wien. klin. Woch.*, 1913, No. 48) reported the treatment of splenic anemia in a young child by injecting cholesterin-esters of olein and palmatin. He reported marked improvement in the blood picture and a diminution in the size of the spleen. STUBER (*Biochem. Zeitsch.*, 1913, li, 211) found that cholesterin diminished the phagocytic activity. Lecithin had no particular effect upon

the phagocytosis but it inhibited the action of the cholesterin. Intravenous inoculation of 70 to 90 c.c. of a 0.5 per cent. to 1 per cent. emulsion of cholesterin reduces the phagocytic index in cats enormously. The reaction may persist for days. On the other hand lecithin slightly increases the index as well as neutralizing the depressing influence of cholesterin previously inoculated. Lecithin heated to 70 degrees reduces its activity. WACKER and HUECK (*Archiv. f. Exper. Path. u. Pharm.*, 1913, lxxiv, 416). Normally the cholesterin in the blood is distributed in the serum as well as the cells. The white cells contain five times as much cholesterin as the red blood cells. The serum contains both free cholesterin and cholesterin esters. The separation of fibrin carries no cholesterin with it. The normal cholesterin content is fairly uniform but is more or less disturbed by diet, muscular activity, and tissue destruction. The feeding of free cholesterin increases the cholesterin and cholesterin-ester content of the blood serum. The same may be observed in the inoculation of cholesterin or oleic acid cholesterin ester underneath the skin. The blood cells play but little part in this alteration of the cholesterin content of the blood. A cholesterin diet leads to the deposition of fat in various organs and cholesterin fat mixtures may be observed in the cortex of the adrenal, liver, lidney, spleen, bone marrow, gall-bladder and adipose tissue. They also found that prolonged muscular exercise led to a diminution of the cholesterin esters in the adrenal while that in the blood was slightly increased, while rapidly fatiguing exercise led to a diminution in the blood serum and a slight increase in the adrenals. FISCHL (*Wien. klin. Woch.*, 1914, No. 27) found an increase of cholesterin in the serum of patients suffering from various dermatoses (urticaria, eczema, mycosis fungoides, xanthoma). He believed that this increase of the cholesterin is associated with a protective reaction of the serum.

Mixed Vaccines against Typhoid and Paratyphoid Fevers.—KABESHIMA (*Centralb. f. Bakt.*, 1914, 74, H. 1) reports upon the use of mixed vaccines as used in the Japanese Marine. A vaccine containing B. typhi, B. paratyphi A and B were administered to many individuals. The local and systemic reaction which followed the inoculation of the mixed vaccine was not greater than that observed in simple ones. In experiment it was shown that the individuals possessed an immunity to infections of each organism and that the use of such vaccines had a definite practical value in the army.

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All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1913 Spruce St., Philadelphia, Pa., U. S. A.

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